

ANNALS of SURGERY

A MONTHLY REVIEW OF SURGICAL SCIENCE AND PRACTICE
ALSO THE OFFICIAL PUBLICATION OF THE AMERICAN SURGICAL
ASSOCIATION; THE SOUTHERN SURGICAL ASSOCIATION; PHILADEL-
PHIA ACADEMY OF SURGERY; NEW YORK SURGICAL SOCIETY.



VOLUME 117
JANUARY-JUNE
1943

EDITORIAL BOARD

- | | |
|---|---|
| WALTER E. LEE, M.D.
<i>Chairman, Philadelphia, Pa.</i> | ROY D. McCLURE, M.D.
<i>Detroit, Mich.</i> |
| BARNEY BROOKS, M.D.
<i>Nashville, Tenn.</i> | GEORGE P. MULLER, M.D.
<i>Philadelphia, Pa.</i> |
| E. D. CHURCHILL, M.D.
<i>Boston, Mass.</i> | H. C. NAFFZIGER, M.D.
<i>San Francisco, Cal.</i> |
| EVARTS A. GRAHAM, M.D.
<i>St. Louis, Mo.</i> | D. B. PHEMISTER, M.D.
<i>Chicago, Ill.</i> |
| ROSCOE R. GRAHAM, M.D.
<i>Toronto, Canada</i> | W. F. RIENHOFF, JR., M.D.
<i>Baltimore, Md.</i> |
| SAMUEL C. HARVEY, M.D.
<i>New Haven, Conn.</i> | A. O. WHIPPLE, M.D.
<i>New York, N. Y.</i> |

JAMES TAFT PILCHER, M.D., Managing Editor

J. B. LIPPINCOTT COMPANY, *Publishers*

PHILADELPHIA

MONTREAL

LONDON

NEW YORK

COPYRIGHT 1943
J. B. LIPPINCOTT COMPANY

MADE IN THE UNITED STATES OF AMERICA

CONTRIBUTORS TO VOLUME 117

ABBOTT, W. E., Cleveland, O.	39
ABELS, JULES C., New York, N. Y.	748
ACKERMANN, WOLFGANG, New York, N. Y.	403
ALDRICH, ROBERT H., Boston, Mass.	576
ALLEN, PHILIP D., New York, N. Y.	473
DE AMESTI, FELIX, Santiago, Chile	183
ARIEL, IRVING, New York, N. Y.	740
ATWATER, JOHN S., Rochester, Minn.	414
AUB, JOSEPH C., Boston, Mass.	834
BANKS, ROLAND W., Philadelphia, Pa.	437
BARCIAM, IRVING, New York, N. Y.	52
BARR, J. HAROLD, Omaha, Nebr.	207
BEECHER, HENRY K., Boston, Mass.	825
BENSON, CLIFFORD D., Detroit, Mich.	268
BERMAN, J. K., Indianapolis, Ind.100, 535.	766
BEST, R. RUSSELL, Omaha, Nebr.	207
BILLINGS, F. T., Nashville, Tenn.670.	677
BINKLEY, GEORGE E., New York, N. Y.	748
BISGARD, J. DEWEY, Omaha, Nebr.	106
BLAKEMORE, ARTHUR H., New York, N. Y.	481
BLODGETT, JAMES B., Boston, Mass.	637
BODENHEIMER, MILTON, New York, N. Y.	52
BRANSFIELD, JOHN W., Philadelphia, Pa.	I
BRICKLEY, WILLIAM J., Boston, Mass.	865
BROOKS, BARNEY, Nashville, Tenn.	728
BROWDER, JEFFERSON, Brooklyn, N. Y.	118
BRUBAKER, ROBERT E., Cleveland, O.	256
BRUCKNER, JOHN P., New York, N. Y.	791
BRUES, AUSTIN M., Boston, Mass.	834
BUCHHOLZ, RANSOM R., Nashville, Tenn.	692
BUTT, HUGH R., Rochester, Minn.	414
CANNON, BRADFORD, Boston, Mass.85.	903
CANNON, IDA M., Boston, Mass.	809
CAPPURRO, RAFAEL, Montevideo, Uruguay	735
CASTEN, DANIEL, New York, N. Y.	52
CHURCHILL, EDWARD D., Boston, Mass.	641
COBB, STANLEY, Boston, Mass.	814
COLP, RALPH, New York, N. Y.	387
COOPER, FREDERICK W., JR., Atlanta, Ga.	718
COPE, OLIVER, Boston, Mass.85, 801, 885, 915.	937
CRAWFORD, ALBERT S., Detroit, Mich.	798
CRUTCHER, RICHARD R., Nashville, Tenn.670.	677

DANIEL, ROLLIN A., JR., Nashville, Tenn.	670,	677
DORRANCE, GEORGE M., Philadelphia, Pa.		1
DOUGLAS, BEVERLY, Nashville, Tenn.		692
DRUCKERMAN, LEONARD J., New York, N. Y.		387
DREYFUSS, M. L., Clifton Forge, Va.		754
EDWARDS, WALDO B., Stapleton, N. Y.		321
EGER, SHERMAN A., Philadelphia, Pa.		355
ELMAN, ROBERT, St. Louis, Mo.		327
EMMETT, J. M., Clifton Forge, Va.		754
ERB, I. H., Toronto, Can.		234
EVANS, EVERETT I., Boston, Mass.		28
EVANS, WILLIAM A., JR., Detroit, Mich.		268
FARMER, A. W., Toronto, Can.		234
FAXON, NATHANIEL W., Boston, Mass.		803
FELL, EGBERT H., Chicago, Ill.		686
FRY, WESLEY, Washington, D. C.		760
GRÖSS, JOSEPH, Cleveland, O.		723
GUBLER, JOHN A., Norfolk, Va.		786
HANNO, HAROLD A., Philadelphia, Pa.		437
HANSELMAN, RUSSELL, Chicago, Ill.		686
HASEMAN, L., St. Joseph, Mo.		468
HERTIG, ARTHUR T., Boston, Mass.		596
HIRSCH, SYDNEY, Cedarhurst, N. Y.		313
HINGSON, ROBERT A., Stapleton, N. Y.		321
HINTON, J. WILLIAM, New York, N. Y.		498
HOLMAN, EMILE, San Francisco, Calif.		315
HOUSER, ALAN D., Indianapolis, Ind.		535
HOWORTH, M. B., New York, N. Y.		278
JOHNSON, GEORGE S., Nashville, Tenn.	74,	134
JOHNSON, ROBERT A., New York, N. Y.		473
JONES, FLORENCE, New York, N. Y.		740
JONES, THOMAS E., Cleveland, O.		256
JOSLIN, ELLIOTT P., Boston, Mass.		607
KERNODLE, H. B., Durham, N. C.		263
KERSHNER, DAVID, Brooklyn, N. Y.		216
KIRSHBAUM, JACK D., Chicago, Ill.		793
KLOPSTOCK, ROBERT, Boston, Mass.		641
KRAFT, GEORGE L., Chicago, Ill.		793
KURTZ, WILLIAM A., Indianapolis, Ind.		535
KYMAN, SEYMOUR, Cleveland, O.		723
LAHEY, FRANK H., Boston, Mass.		332
LEE, H. F., Philadelphia, Pa.		348



CLEFT PALATE

GEORGE M. DORRANCE, M.D., AND JOHN W. BRANSFIELD, M.D.

PHILADELPHIA, PA.

IN 1925, Dorrance proposed the so-called "push-back" operation. This operation was devised to obtain complete velopharyngeal closure—a condition essential in any cleft palate operation to assure a normal voice control. In 1927, he emphasized the fact that early cleft palate operations, *i.e.*, before the fourth year, frequently failed in whole or in part. We have frequently stated that patients upon whom three or four operations were necessary to obtain closure of the cleft palate have hard, fibrous, inflexible palates. This invariably leads to poor phonation.

We felt at that time (1927) that there were quite a few cases where the palate could not be brought back to the posterior wall of the pharynx. With passing years, this group has been greatly reduced.

While we are sure that the "push-back" operation overcame one of the chief faults of the standard cleft palate operations, *viz.*, a short palate, we were keenly aware that perfection had not been obtained. The hole left in an anterior palate in complete clefts or in unilateral lip-jaw splits, even when a good fitting plate was used, was an affront to the surgical mind.

Progress was made, from time to time, by varying procedures—some of them previously proposed by other surgeons and others devised or modified by us to conform with problems occurring in the "push-back" operation. We are reporting on two distinct additional procedures, both of which, during the past five years, have given very satisfactory results.

The first of these is the use of the mucoperiosteum of the vomer. We find that Lannelongue, in 1872, was the first to utilize a portion of the vomerine mucoperiosteum to close off the nose from the oral cavity. He dissected the mucoperiosteum, leaf-like, from one side of the vomer, and sutured the free end under the palatal mucoperiosteum. Veau sutures the vomerine flap to the nasal mucous membrane and covers part of the mucous membrane with a palatal flap. In the light of our experience, we find it is much easier, and surer, to obtain raw surface-to-raw surface by suturing the vomer flap under the palatal tissue (Figs. 1, 2, 3 and 4). We see no advantage in adding a palatal flap, as it complicates later operations.

The value of vomer flap procedure in "push-back" operations was ob-

FIG. 1.

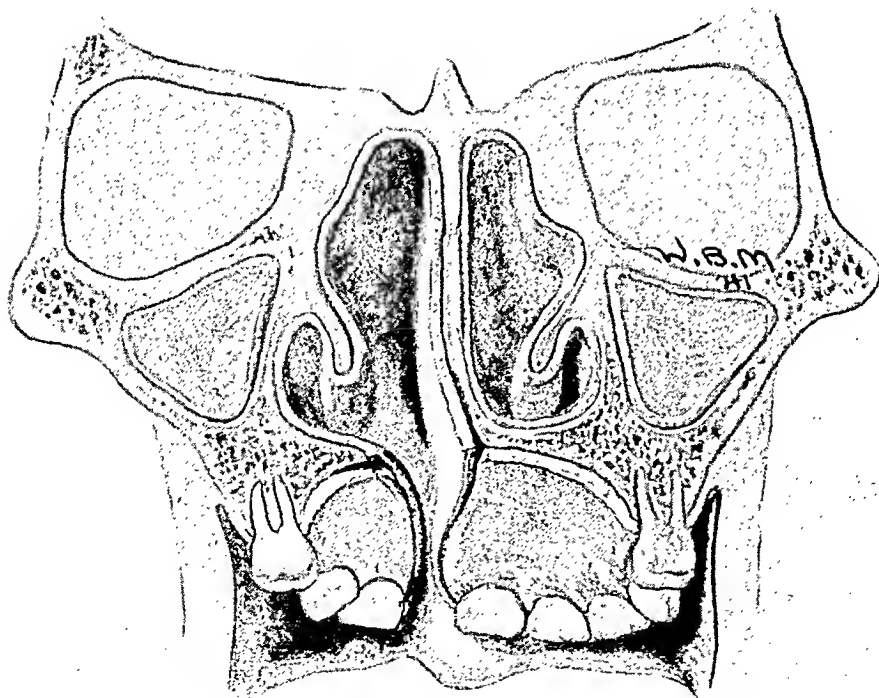
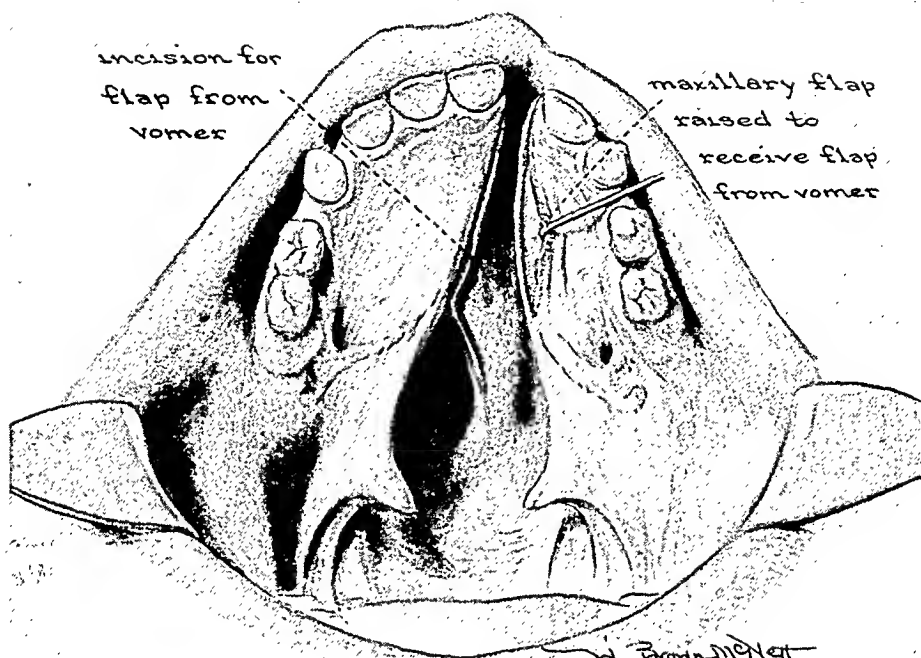


FIG. 2.

FIG. 1.—Incision for the vomer flap.

FIG. 2.—Transverse view of the incision and elevation of the flaps from the vomer.

FIG. 3.

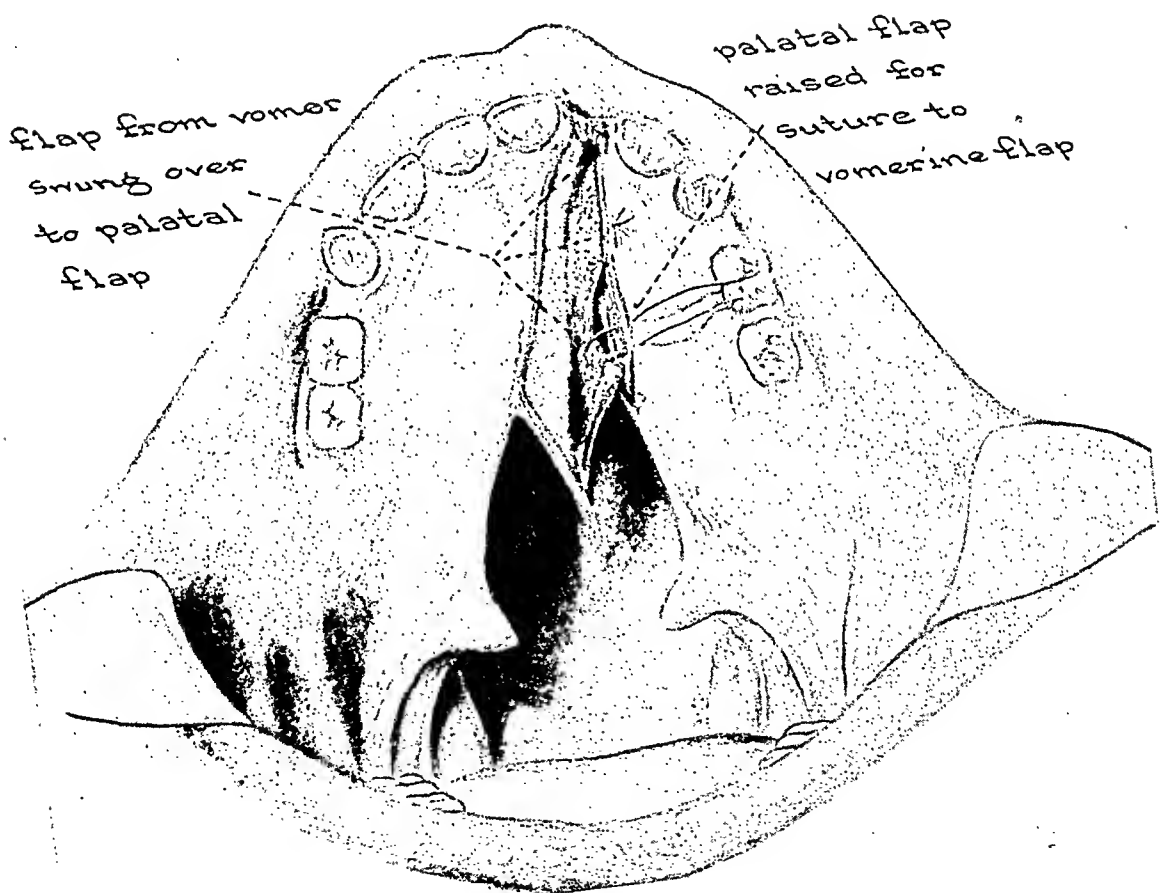
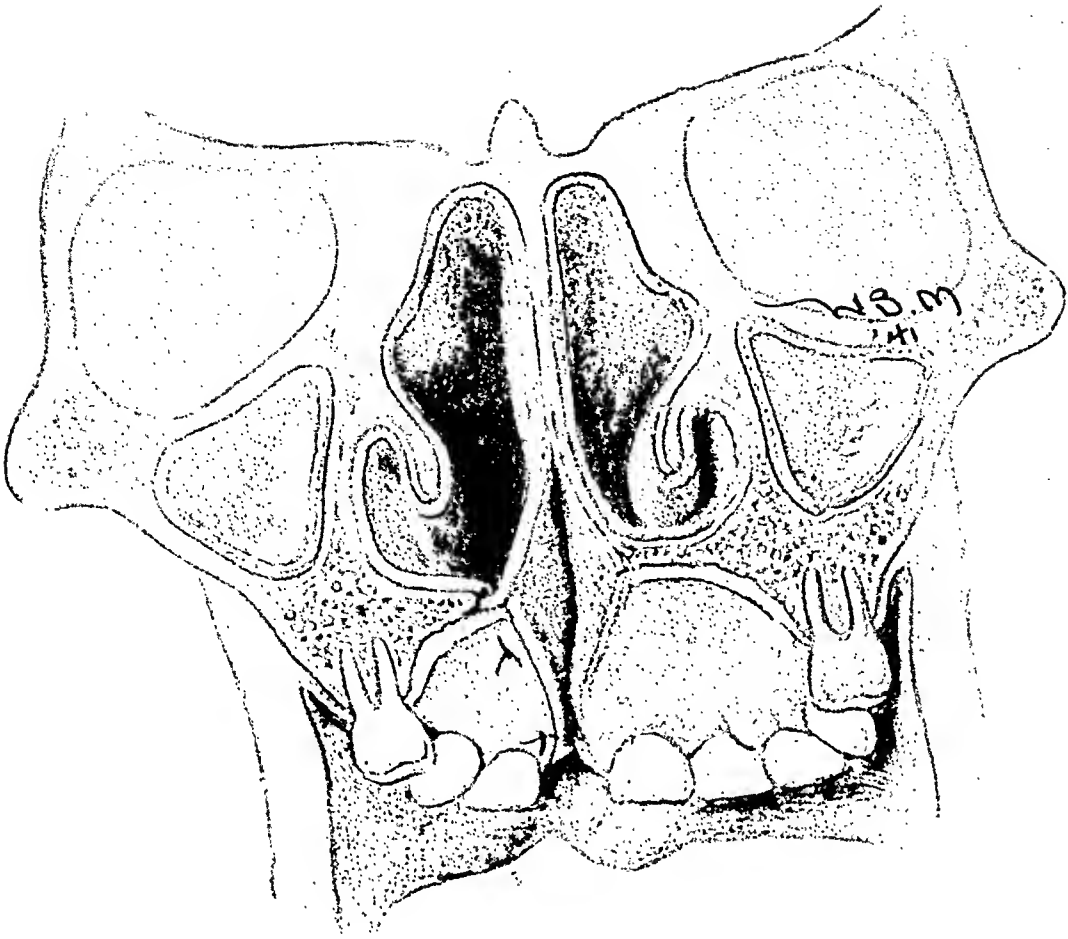


FIG. 4.

FIG. 3.—Transverse view of the completed vomer flap.

FIG. 4.—Suturing of the flap in the vomer transplantation.

FIG. 5

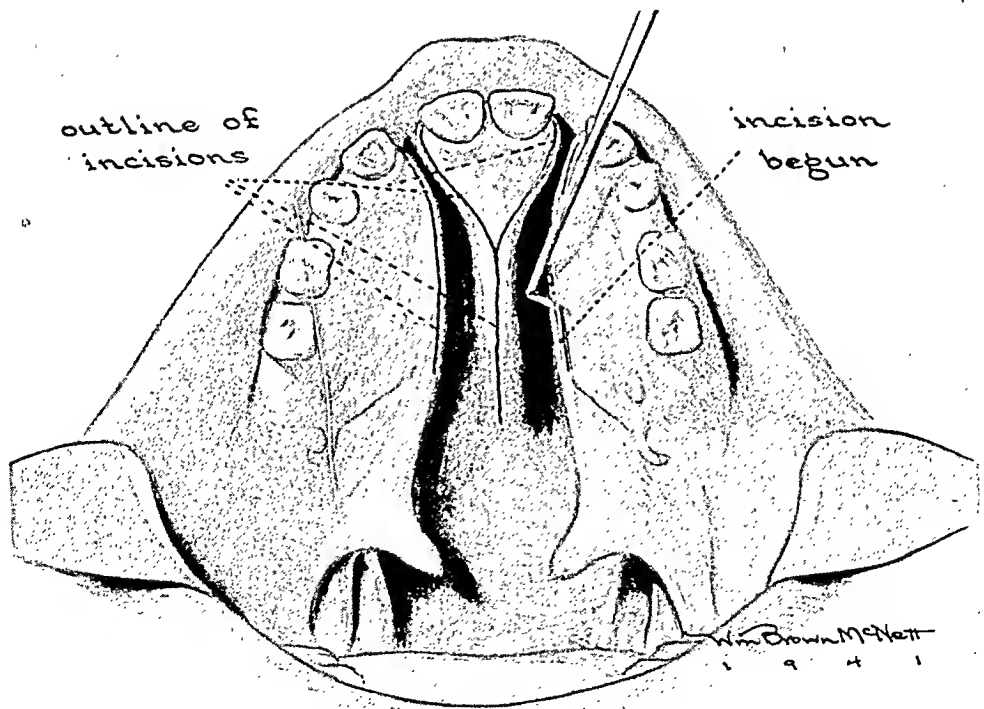
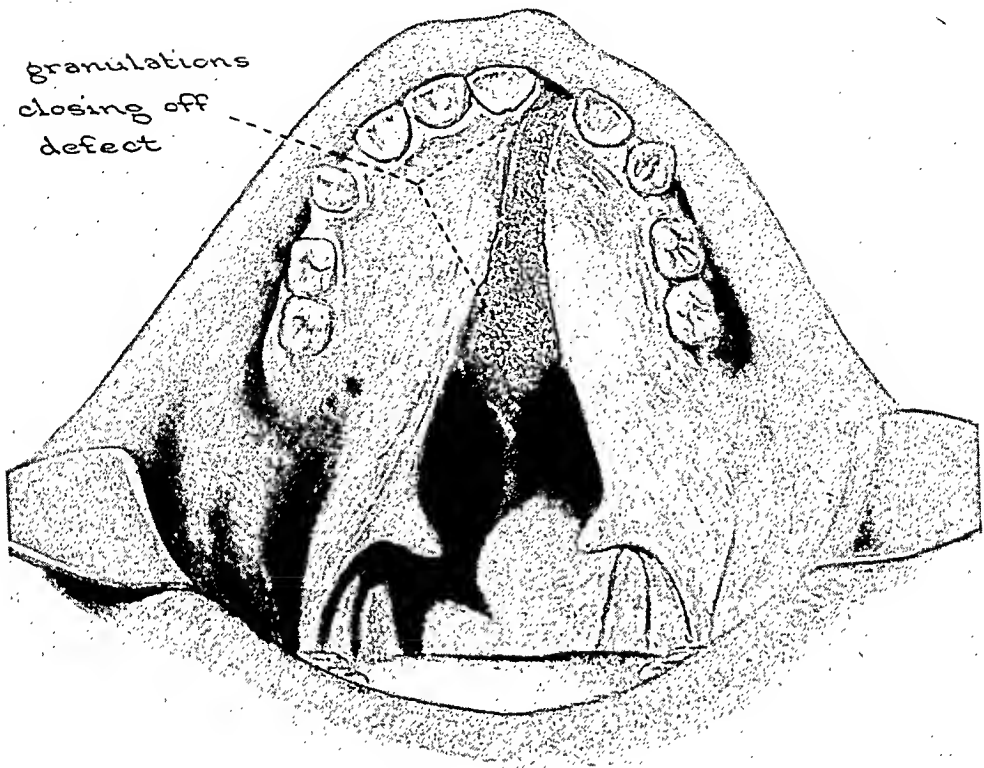


FIG. 6.

FIG. 5.—Completed and filled in vomer-flap operation in single lip-jaw palate cleft.

FIG. 6.—Lines of incision for bilateral vomer flaps in a double lip-jaw palate cleft. Note how far forward they may be placed.

vious and if, in addition, we could fill up the cavity formed with granulation tissue, we would greatly enhance the operation. This was achieved by packing the area with iodoform gauze, and holding it in place, as shown in Figure 10. In double, complete cleft palate, Pickler advised the double vomerine flap. We have used this, extending the flaps further anteriorly. We have had no failures in obtaining a granulating surface, which usually fills in flush with the palatine bones (Figs. 2 to 10 inclusive).

The second addition to the original "push-back" operation is the lining of the palatal mucoperiosteum flap with a Thiersch or split-skin graft: A split- or Thiersch skin graft is sutured in place under each flap raw surface-to-raw surface (Figs. 17, 18, 20, 23, and 28). Since adopting this procedure, crust formation has been diminished. The contracture of flaps when finally displaced backward in the second stage is either completely eliminated or greatly minimized. In order to assure a take, pressure on the flap is necessary. This is accomplished by placing iodoform gauze over the flaps. The gauze is maintained at a constant fixed pressure by strands of silver wire inserted between the posterior teeth and then carried across the palate to pass between the last two teeth on the opposite jaw; the ends are then carried across the mucous membrane above the incisor teeth; the ends of the wire are twisted together and bent back across the palate, being held in place under the horizontal wire which passes between the posterior teeth (Fig. 10). In our last 10 cases we have substituted a splint designed for us by Dr. P. Gross. It is described in the *American Journal of Orthodontia and Oral Surgery*, September, 1942. The wire and gauze are removed in 10 to 12 days.

While each cleft palate requires special modifications of technic, one can outline specific procedures which will be applicable to each type commonly met with:

TYPE I—CONGENITAL SUBMUCOSAL OR CONGENITAL INSUFFICIENCY OF THE PALATE AND CLEFT OF THE SOFT PALATE

The shortening in these types of cleft palate is almost invariably due to a deficiency of the horizontal plate of the palate bone (Fig. 11). Since the soft palate is attached by the palatine aponeurosis to the shortened horizontal plate, the shortening is in direct proportion to the bony deficiency. Obviously, the simple repair of any cleft in the soft palate cannot have the slightest effect in accomplishing velopharyngeal closure.

We advise, and routinely carry out, the following procedures: (1) We attempt to find the amount of bone deficiency by the insertion of a needle at various points, as shown in Figures 12, 13 and 14. (2) In all cases, we perform the two-stage "push-back" operation.

FIRST STAGE OF THE "PUSH-BACK" OPERATION

The first stage consists of raising the flap by Method A, Fig. 15, or B, Fig. 19. Method A is selected if we are dealing with a fairly normal, well-developed flap with adequate blood supply. In these cases, the palatine vessels

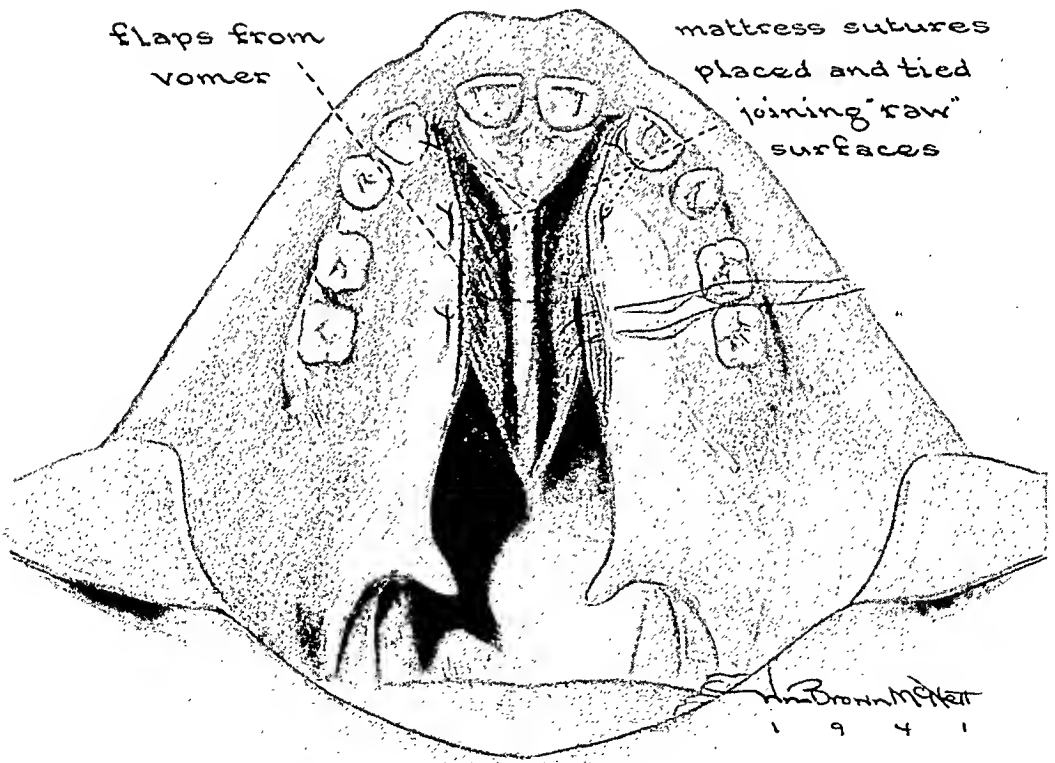
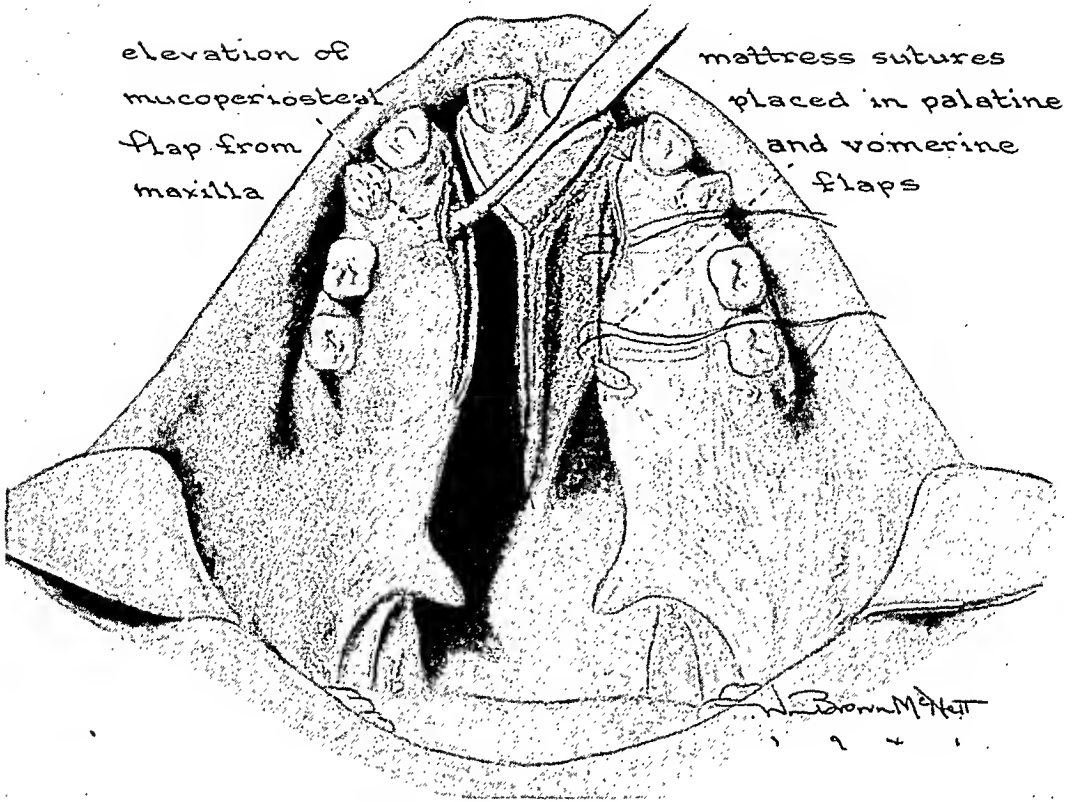


FIG. 7.—Demonstrating the method of elevating and suturing the vomer flap in double lip-jaw palate cleft.

FIG. 8.—Completed double vomer flap in double lip-jaw palate cleft.

are divided (an absolute necessity to obtain sufficient backward displacement). When the flap is raised, a skin graft is sutured in place on the palatine mucoperiosteum, as shown in Figures 16, 17, and 18. The flaps are returned to their bed and the edges sutured. In some cases where the palatine mucosa is thin, or where a considerable bony defect is present, or where the blood supply does not appear to be adequate, Method B is employed (Fig. 19). In those cases, the palate is raised, leaving a bridge of undivided tissue to insure blood supply. The remaining portion of the flap is freed completely from the bone and the palatine arteries are divided, as in Method A. The flaps are then sutured back in their normal position.

We have noted that the flaps thicken appreciably following this procedure. If, when the second stage is being performed, we find the flaps

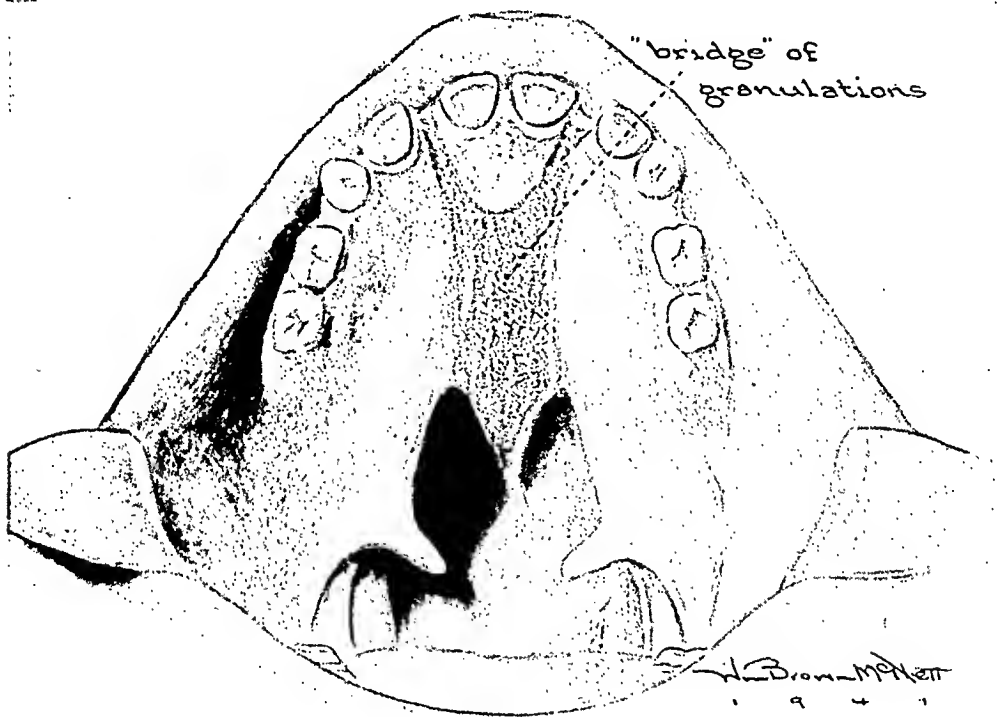


FIG. 9.—Final results of the vomer flap in bilateral lip-jaw palate cleft.

are not of sufficient thickness, we raise them and again replace them and wait for another four or ten weeks before elevating and placing the skin grafts, after the method outlined above.

We deliberately avoid using the nasal mucous membrane, because in performing the second stage of the "push-back" operation it is necessary to divide the nasal mucous membrane and aponeurosis at its attachment to the bone, thus leaving a raw area. If the nasal mucous membrane is not divided, complete velopharyngeal closure will not be obtained in many cases because the muscles responsible for this closure will not be restored to their normal position.

SECOND STAGE OF THE "PUSH-BACK" OPERATION

A flap is raised through the former incision, the nasal mucous membrane

being divided from the posterior bony palate (Fig. 20). The hamular process is then divided, thus transposing the tensor palati muscle from a tensor to an elevator muscle. The incision is continued around the tuberosity of the maxilla and over the pterygomandibular fold, freeing the palate from all bony attachments.

The uvula now rests on the posterior pharyngeal wall. The anterior portion of the flap is sutured to the fibrous membrane at the apex of the defect, and is also immobilized by passing one or two aluminum-bronze wires first through the bony palate, then through the apex of the flap on either side of the midline. Each wire is then twisted until the flap is held securely; the ends of the wire are then bent back, thus preventing any injury to the flap and tongue (Fig. 21).

The bony palate and lateral sulci, now devoid of their covering as a result of the push-back operation, are covered and packed with iodoform

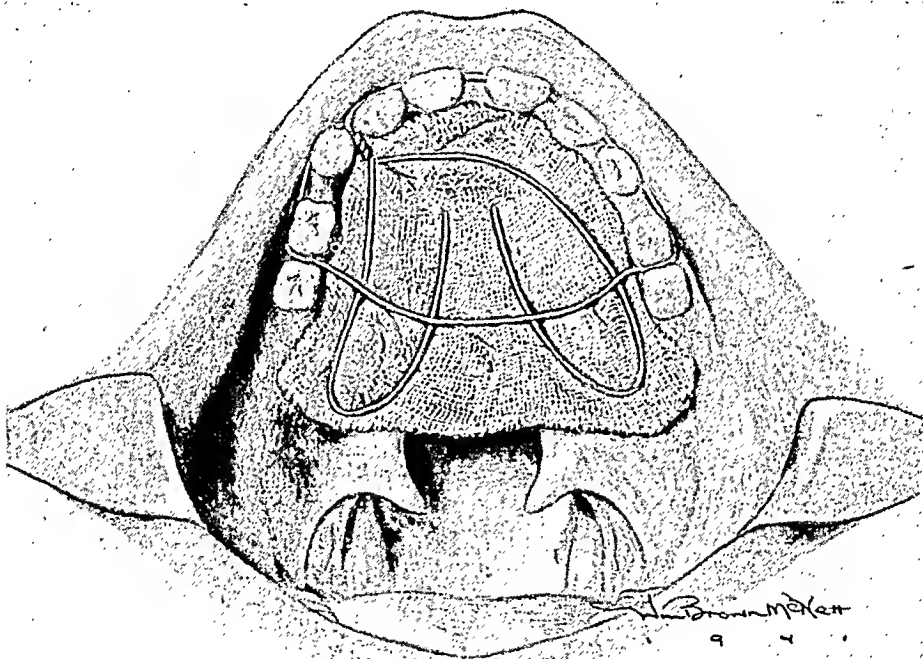


FIG. 10.—Method of placing silver wire to hold the iodoform gauze in place.

gauze, which is held in place by a strand of silver wire inserted as previously described (Fig. 10). The gauze is allowed to remain in place 10 to 14 days.

A summary of the necessary steps involved in the correction of congenital insufficiency of the palate follows:

Method A.—1. Raise the flap and suture the skin graft in place. 2. Three to ten weeks later, perform the “push-back” operation. Method B.—1. When the viability of the palatal tissue is uncertain, a three-stage operation should be performed. First raise the palatal flap, divide the palatine vessels, and suture the flap back in place. 2. Six to eight months later, raise the flap through the original incision and insert the skin graft. 3. Three to ten weeks later, complete the repair with the “push-back” operation.

TYPE II—CLEFT OF THE SOFT PALATE

This group of defects presents not only a short or insufficient palate but, in addition, a cleft of the soft palate (Fig. 12). The operation of choice in these cases is the two-stage "push-back" operation (Fig. 16).

The second stage of the "push-back" operation is now accomplished by raising the flap, dividing the hamular process on either side, severing the connections of the soft palate from the nasal surface of the bony palate. In this way, the nasal mucous membrane and the aponeurosis are separated from the posterior border of the hard palate (Fig. 20).

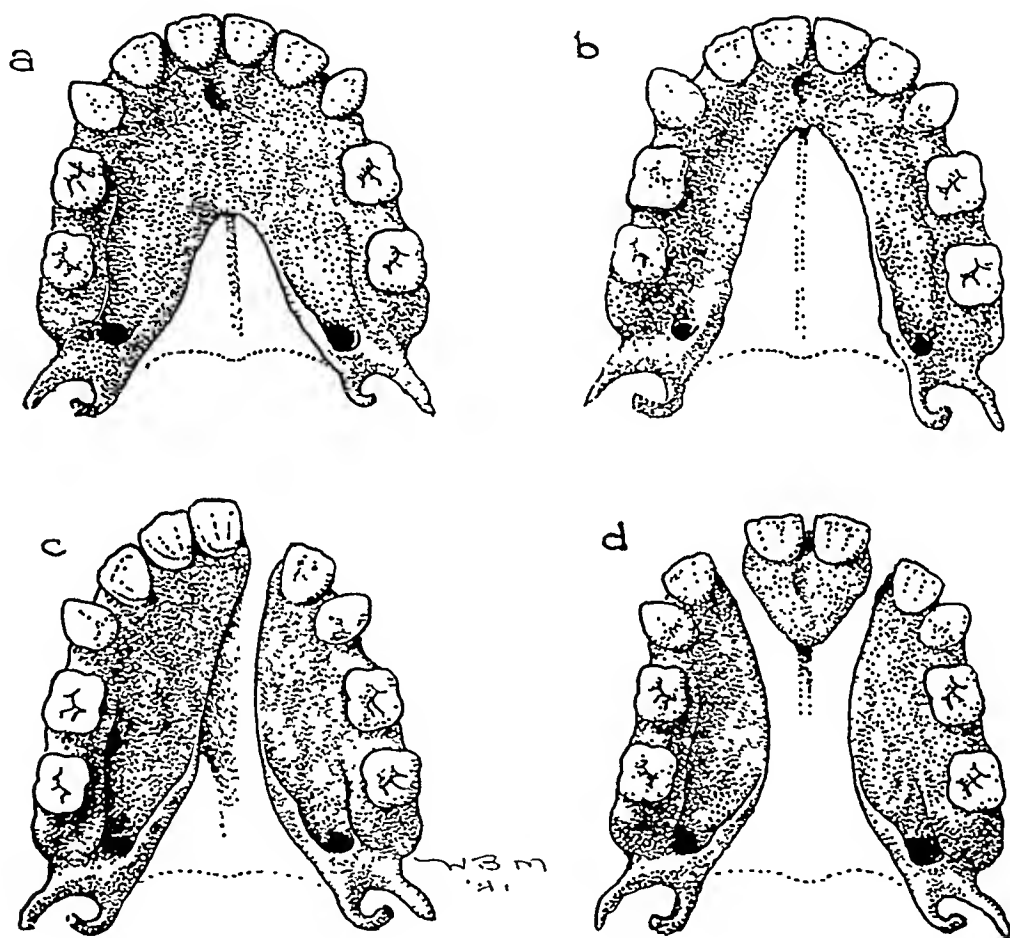


FIG. 11.—Deficiency of the bone in different variations of cleft palate.

The next step is to denude the edges of the cleft and approximate the nasal muscous membrane of the two halves, with interrupted sutures (left untied) (Fig. 21). It will be found helpful to insert a few mattress sutures to evert the edges and prevent inversion of edges—a frequent cause for nonunion. One or two Veau sutures are next placed through the muscular layer at the middle third of the soft palate. We use a specially designed needle for placing this intramuscular suture, bringing it from the midline out through the lateral incisions, as shown in Figures 21 and 22, and ending in midline. These needles—straight or curved—with wire sutures attached, are prepared for us by the Davis and Geck Co. The suture is placed and left untied; the nasal sutures are tied, closing this surface, with the edges everted.

The Veau suture is now twisted (tied) bringing the two halves of the cleft into good approximation, without tension. The oral sutures are next inserted and tied. These sutures should pass down to, but not through the nasal mucosa. Ordinary through-and-through sutures, if not carefully laid and tied, will invert the edges of the mucous membrane. Use end-on-end mattress sutures. The anterior end of the flap is now sutured to the palate bone or to the fibrous tissue present. An iodoform pack is placed over the uncovered palate and in the lateral incisions (Fig. 10).

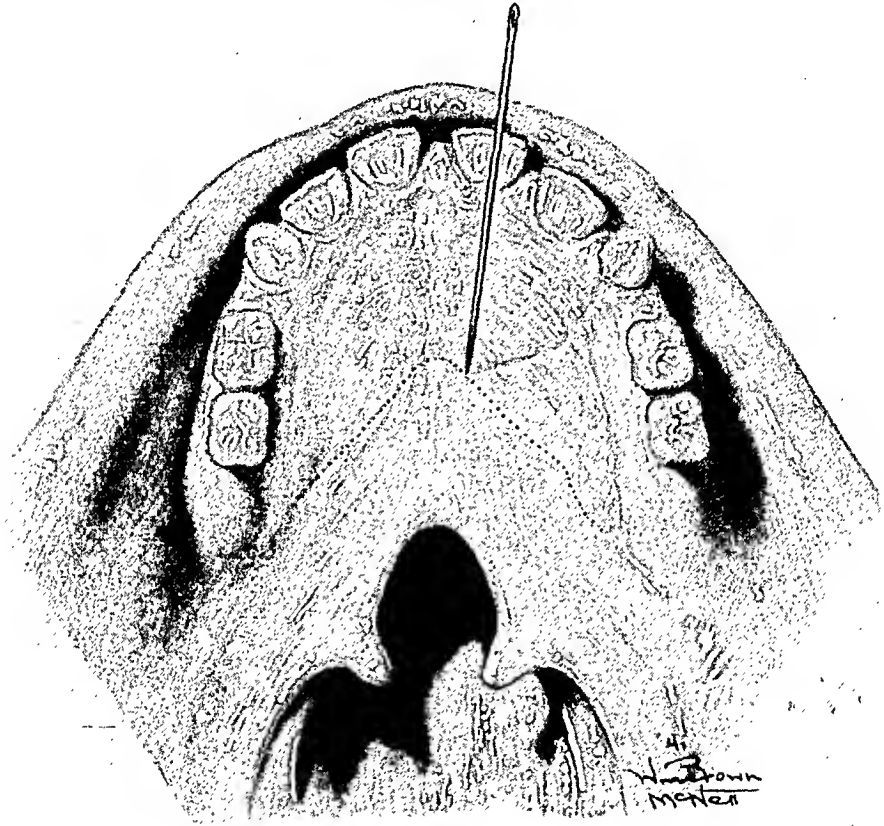


FIG. 12.—Determining the bone deficiency.

The raw nasal surface that formerly existed in the "push-back" operation is avoided by the use of the skin graft (Fig. 23). Tension sutures, or metal plates, used to reduce tension will frequently produce a permanent scar. Intramuscular and intrafascial sutures are well tolerated and, for this reason, the Veau suture is ideal. We use it in all cases. The mattress suture is well tolerated because it gives maximum approximation of the two muscular segments with epithelial or surface tissue compression.

A summary of the operative procedure in this type is: 1. Raise the flap and suture a skin graft in place. 2. Three to ten weeks later, the "push-back" is completed.

If the palatal tissues do not warrant extensive surgery at this time, a three-stage procedure should be employed:

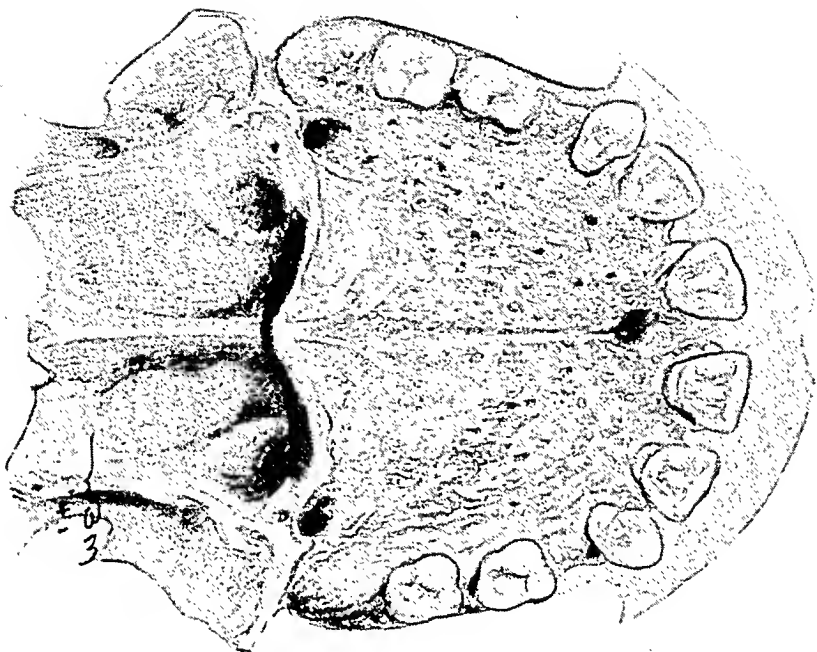


Fig. 13.—Normal bones in the palate. (Red border indicating where the palatine aponeurosis should be attached).

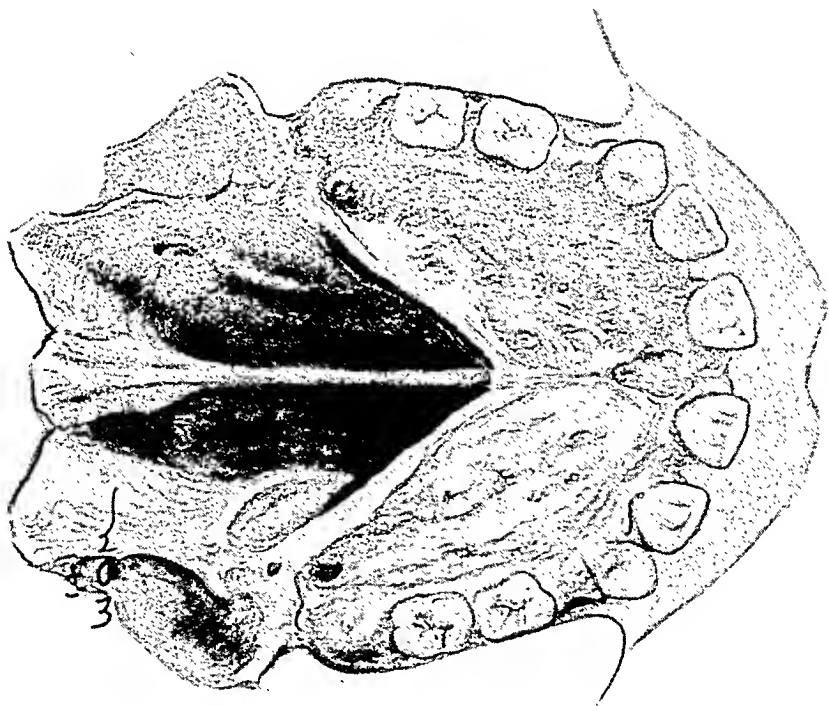


Fig. 14.—Note the loss of bone in a submucous or cleft of the soft palate. (Rough area is where aponeurosis would be retracted to, thus shortening the palate).

FIG. 15.

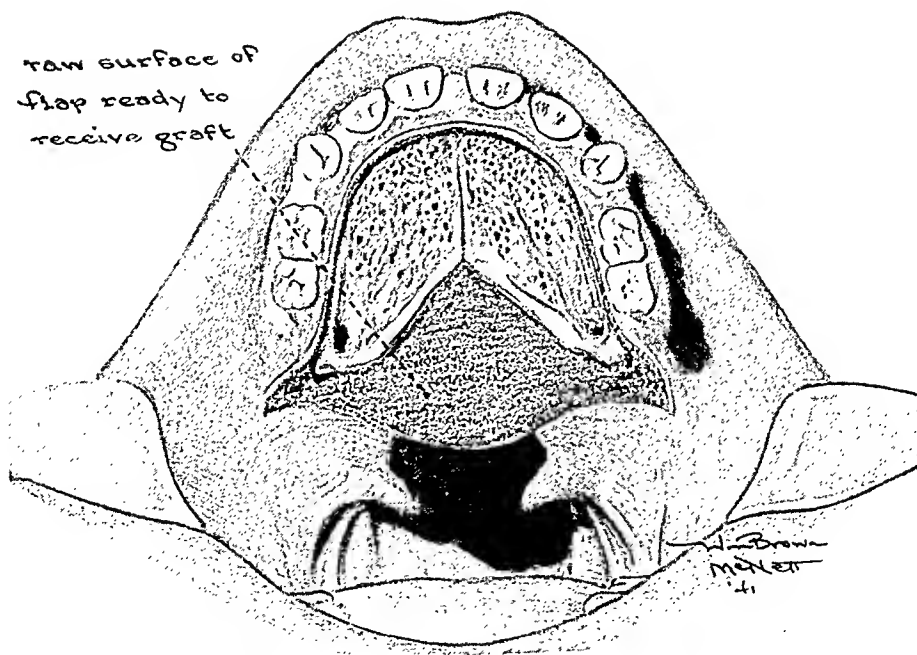
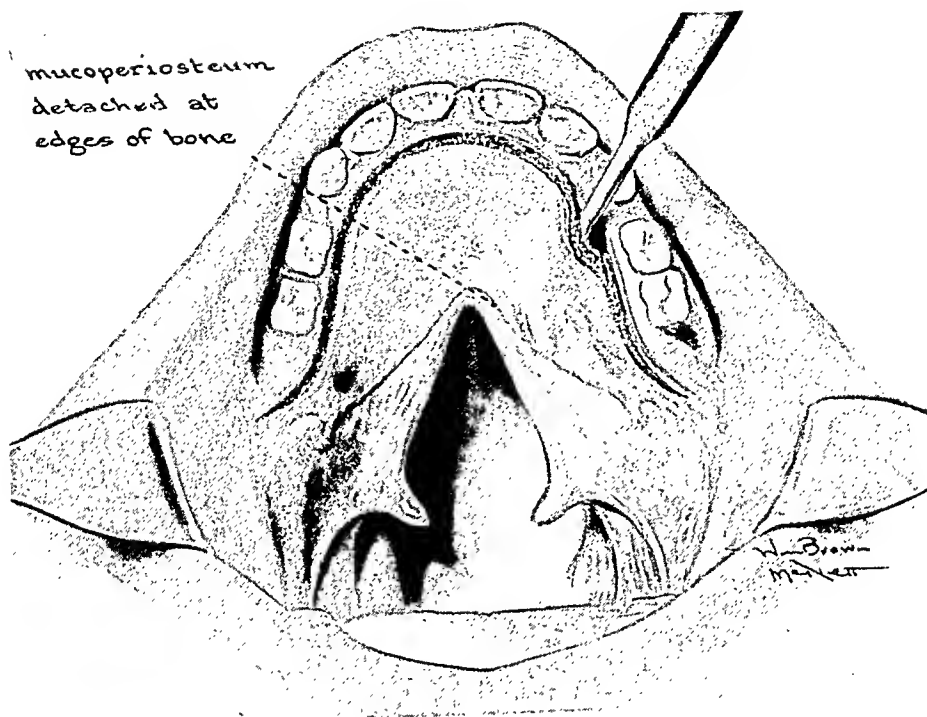


FIG. 16.

FIG. 15.—Method A—For elevation of the mucoperiosteal flap.

FIG. 16.—Flap elevated—Vessels divided ready for skin graft.

FIRST STAGE: Raise the flap, sever the palatine vessels and suture back in place.

SECOND STAGE: Six to eight months later, raise the flap through the original incision and insert the skin graft—resuture.

THIRD STAGE: Three to ten weeks later, perform the “push-back” operation.

TYPE III—CLEFT OF THE SOFT AND HARD PALATE
UP TO THE PREMAXILLA

This group presents four distinct variations: 1. The defect in the palate bone may be as wide as the cleft in the soft palate. 2. The margins of the soft palate cleft may converge anteriorly into the narrow cleft of a very poorly developed hard palate, with its characteristically high narrow arch. 3. The vomer may be fairly well developed or only rudimentary.

In our experience, the vomer is usually rudimentary and does not approach the level of the defect. These variations affect the type of operative procedure. The presence or absence of a normal vomer is the most important factor present. When the vomer is rudimentary, as is usual in this type of cleft, it plays no part in the correction. The Langenbeck lateral incision may be made, the flaps raised and the skin grafted in one operation. Three weeks later, the Langenbeck operation is performed closing the cleft. Six months later, the V-“push-back” operation is performed.

The Wardill operation uses the Veau-method of stretching the mucous membrane and covering it with V-flaps, much the same as we do in the V-“push-back.” If the vomer is well developed, we perform the “push-back” as described in Type V.

The practicability of the Veau idea of reflecting the nasal mucous membrane must be considered. When the arch is high and narrow, the mucous membrane is difficult if not impossible to transfer. When closure is obtained in this type, it is not entirely satisfactory. In a limited number of cases where the cleft is not too wide or the arch is not too high, it is possible to elevate sufficient nasal mucous membrane from the floor of the nose to suture it in the midline. It has not been entirely satisfactory for us. We feel, however, that the skin graft reduces the possibility of tissue failure to a minimum and preference is made of its use.

TYPE IV—SINGLE COMPLETE CLEFT OR UNILATERAL
LIP-JAW PALATE SPLIT

When conditions permit, the lip is closed soon after birth. This produces a fusion of the alveolar cleft. Rarely, in this type, is the vomer rudimentary. As a rule, it is well developed and attached to the longer side and its mucoperiosteum can be used to close off the nasal chamber.

In the presence of a well developed vomer, lying on a plane and articulating with the palatal process, its mucosa may be separated from the bone and reflected like the open page of a book. This leaves the vomer devoid of its mucosal covering. The palatal mucous membrane on the short side

FIG. 17.

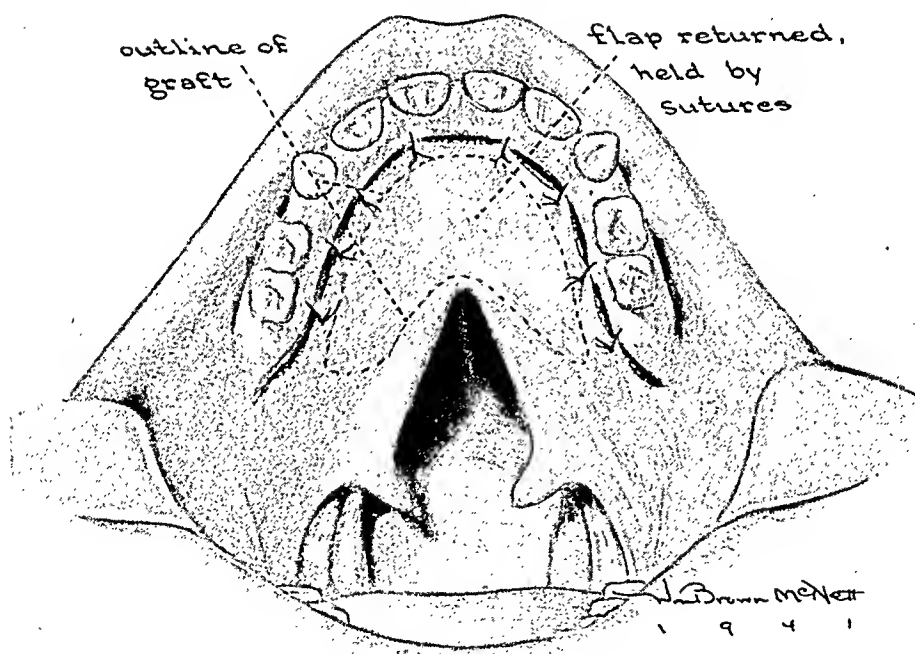
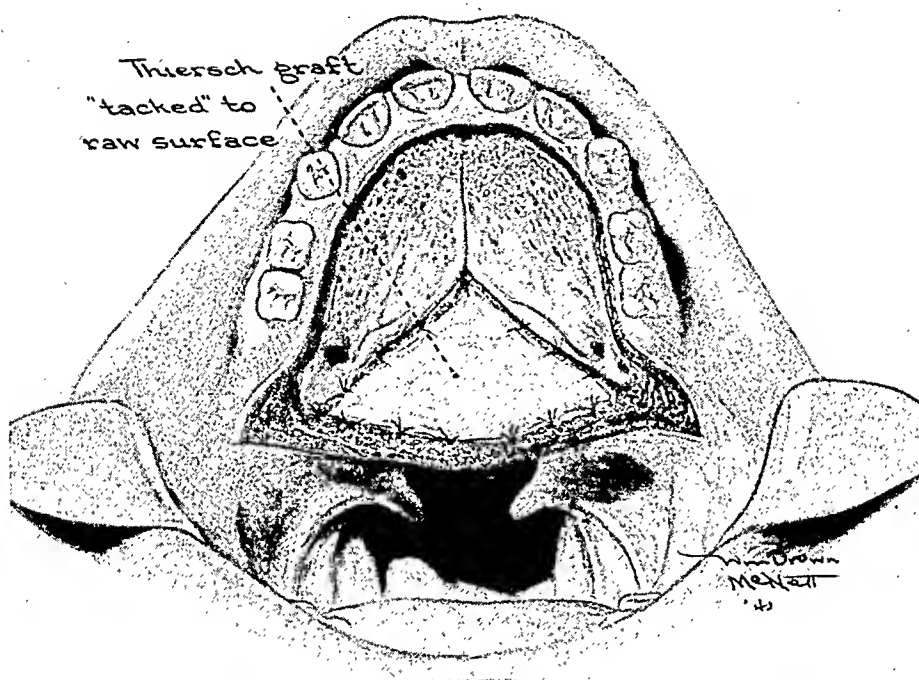


FIG. 18.

FIG. 17.—Flap elevated—Skin graft sutured in place.

FIG. 18.—Flap with skin graft resutured in place.

CLEFT PALATE

FIG. 19.

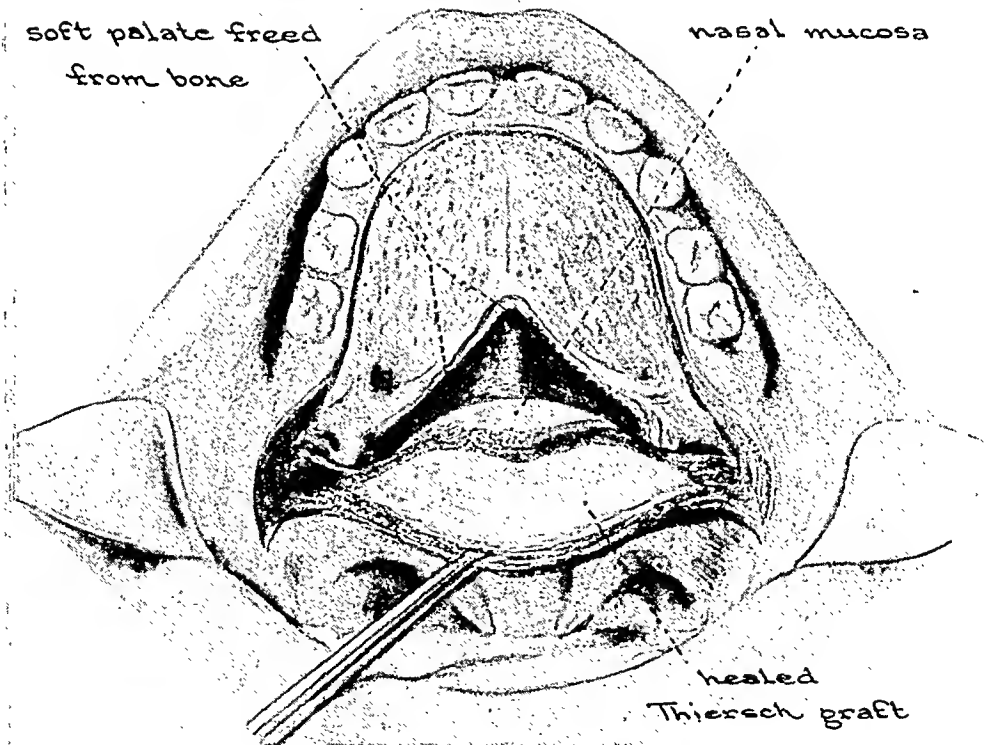
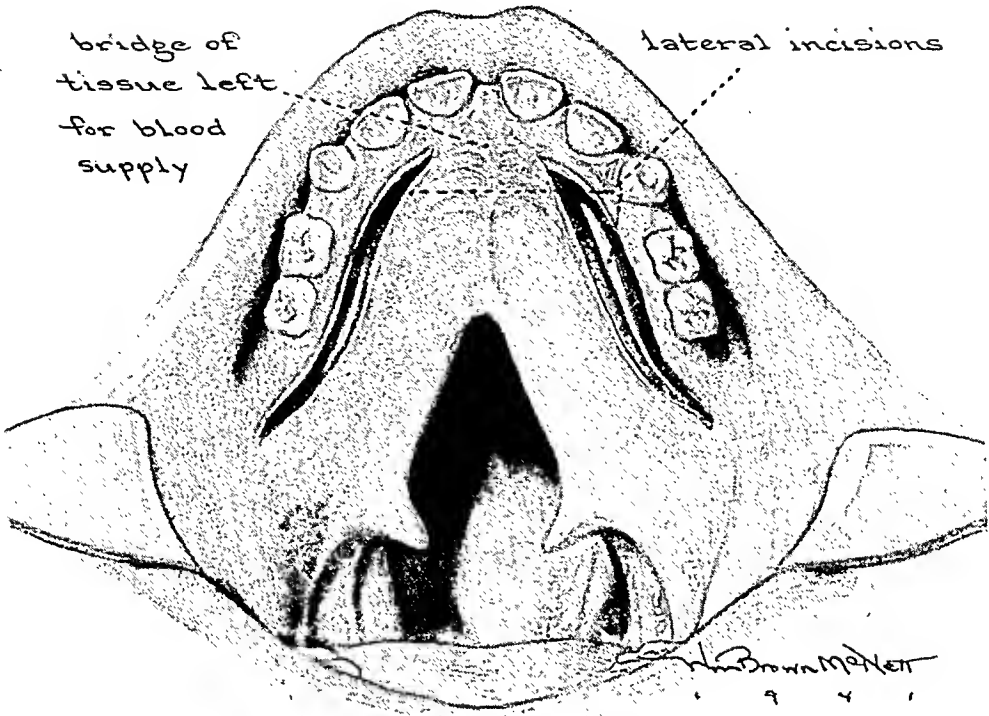


FIG. 20.

FIG. 19.—Method B—For elevation of the mucoperiosteal flap.

FIG. 20.—Flap elevated showing a successful skin graft in a cleft of the soft palate.

FIG. 21.

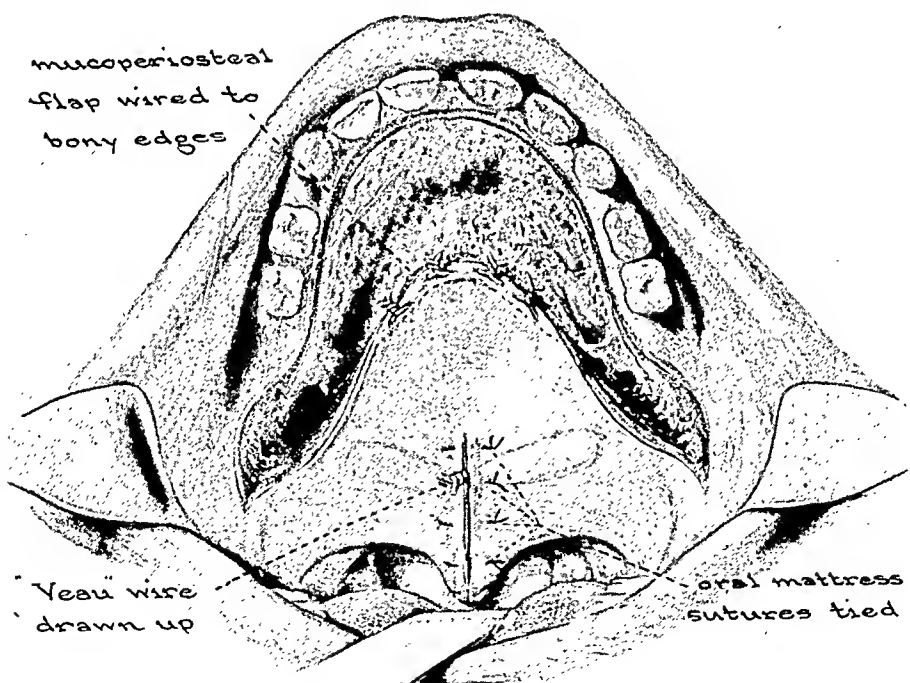
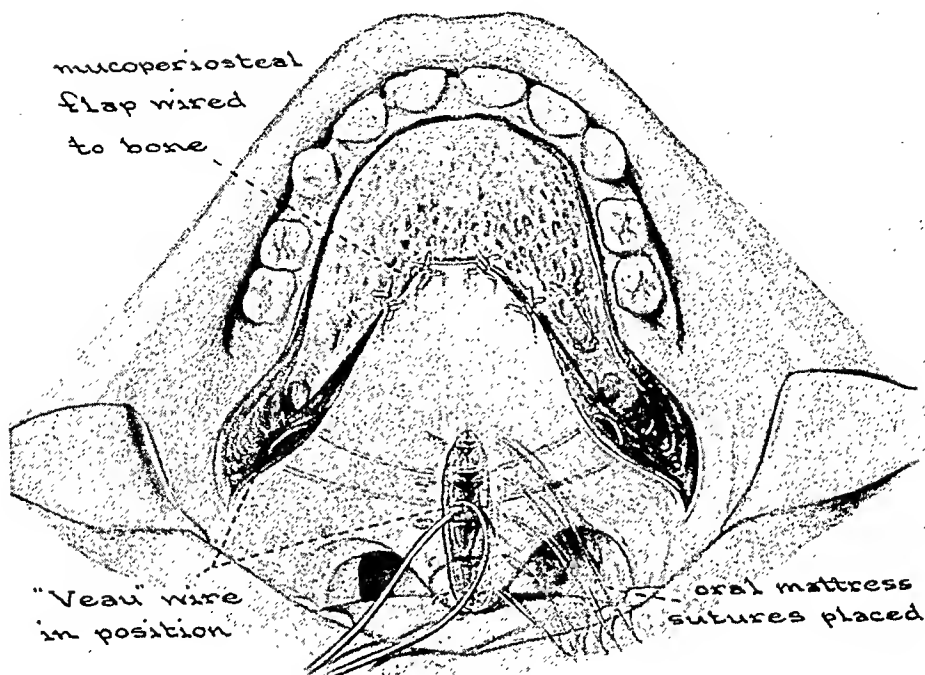


FIG. 22.

FIG. 21.—Final stage of the "push-back" operation in cleft of the soft palate.

FIG. 22.—Final stage of the "push-back" operation.

is elevated one-quarter inch along the margin of the cleft and the vomer flap is tucked into this recess. This brings the two raw surfaces into contact in which position they are immobilized with mattress sutures. The triangular cavity thus created is packed with iodoform or xeroform gauze, and held in place by a wire around the teeth for at least ten days. This area granulates progressively to the surface, effectively solidifying the anterior third of the palate (Figs. 1, 2, 3, 4, 5 and 10).

The operative sequence for correction in the presence of a well developed vomer is as follows: About the second or third year, or later, the vomer flap is reflected as described, and the area allowed to fill in. In from five months to two years later, a first of a two-stage "push-back" operation is performed. This consists of a long lateral incision on either side; the posterior palatine vessels are divided and the flaps raised (Fig. 25). If they blanch, and if very thin, we immediately suture them back into place. If the flaps are of normal thickness we suture in place skin grafts and then suture the flaps back in place. Three to ten weeks later, the "push-back" operation is performed. The flaps are elevated with their adherent skin grafts, carried backward and fixed. The pattern of this reconstructed palate resembles that of Smith, Ganzer, Halle-Ernst, Limberg and Wardill (Fig. 26).

It should be noted here that the filled-in area, bounded by the vomer flaps, remains untouched. Incisions for the "push-back" flaps are made only when the bony palate has been unmistakably outlined with a needle. This gives a bony floor for the flaps on either side of the vomer area, and the "push-back" operation is completed essentially the same as previously described.

To summarize briefly: The vomer flap is raised and sutured "leaf-of-the-book-wise" to the opposite palatal flap. The space formed is packed and allowed to granulate to the surface. We strongly stress this phase of the operation, because the anterior part of the hard palate has automatically repaired itself without disturbing any of the palatal tissue.

Five months after the vomer-mucoperiosteal transplant, the tissue in this area is usually well organized and the flaps may be elevated and skin graft inserted. Three to eight weeks later, the "push-back" operation is performed. The order of the repair is as follows:

1. The nasal sutures are inserted but not tied.
2. The Veau suture is inserted but not tied.
3. The nasal sutures are now tied.
4. The oral sutures are inserted but not tied.
5. The Veau suture is now tied by twisting the ends, thus approximating the two halves.
6. The oral sutures are now tied.
7. Retroposition is effected, and the palate is anchored in its new position with the wire sutures as previously described.

The bony palate is covered with iodoform gauze, and the latter is held in place with silver wire to permit granulation across this space.

The unilateral lip-jaw palate split, with a rudimentary vomer, is rare, but in such cases the repair may be made by either of two methods:

1. The Langenbeck operation is performed as a preliminary step, with or without a skin graft, as conditions warrant.
2. Use the method of Ganzer, modified by Limberg, and popularized by Wardill (Fig. 24).

We prefer the Langenbeck method of anterior closure followed by the V-"push-back" operation.

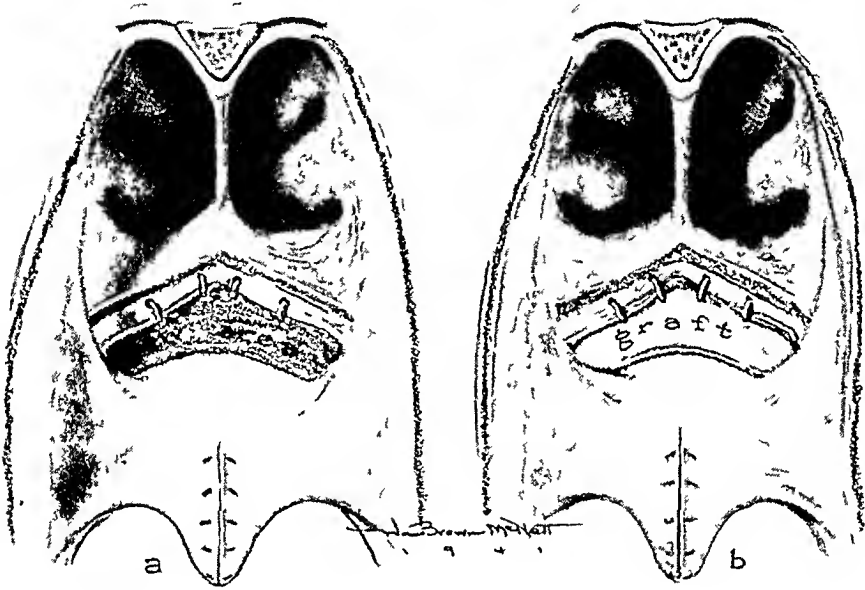


FIG 23—Nasal surface after the "push back" operation (a) Without skin graft (b) With skin graft in place.

If the flaps permit, the grafts are inserted at the same time the palatal mucous membrane is raised. If, on the other hand, the tissue is very thin and blanches, a three-stage operation is automatically resorted to in completing the Langenbeck procedure. Since a short palate now exists, the V-"push-back" operation is performed, much the same as shown in Figure 26, to obtain velopharyngeal closure.

TYPE V—DOUBLE COMPLETE CLEFT OR BILATERAL LIP-JAW PALATE SPLIT

The method of closure is by reflecting of one or both vomer flaps of mucous membrane outward as the open pages of a book (Figs. 6 and 7). It is easier to do this bilaterally at once, and not in stages. Some authors believe there is danger of losing the vomer if this is done. However, our experience has not borne this out.

Upon the first examination of a cleft palate, soon after birth or in infancy, the vomer may appear to be only a remnant. A year or so later,

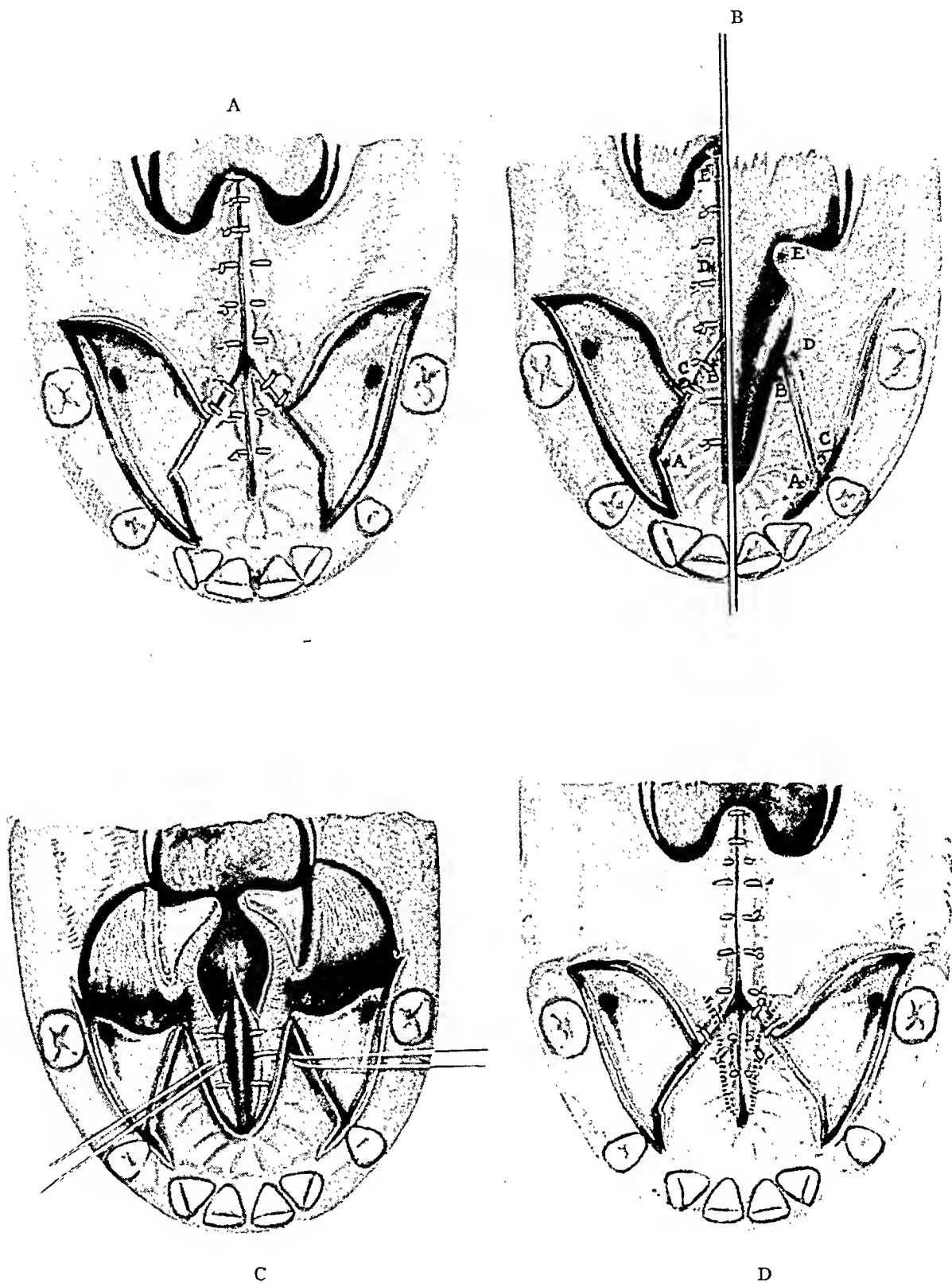


FIG. 24.—Wardill's method of operation. (A) Completion of the suture line. (B) Illustrates diagrammatically how, by cutting flaps in the method described, a form of VY advancement of the velum takes place. The letters indicate corresponding positions before and after operation. (C) The mucosa from the nasal surface of the hard palate is united to the vomerine mucosa. The situation of the stay sutures is shown. (D) Repair completed. The dotted line shows the approximate of the united nasal mucosa. (British Journal of Surgery, 25:1937)

FIG. 25.

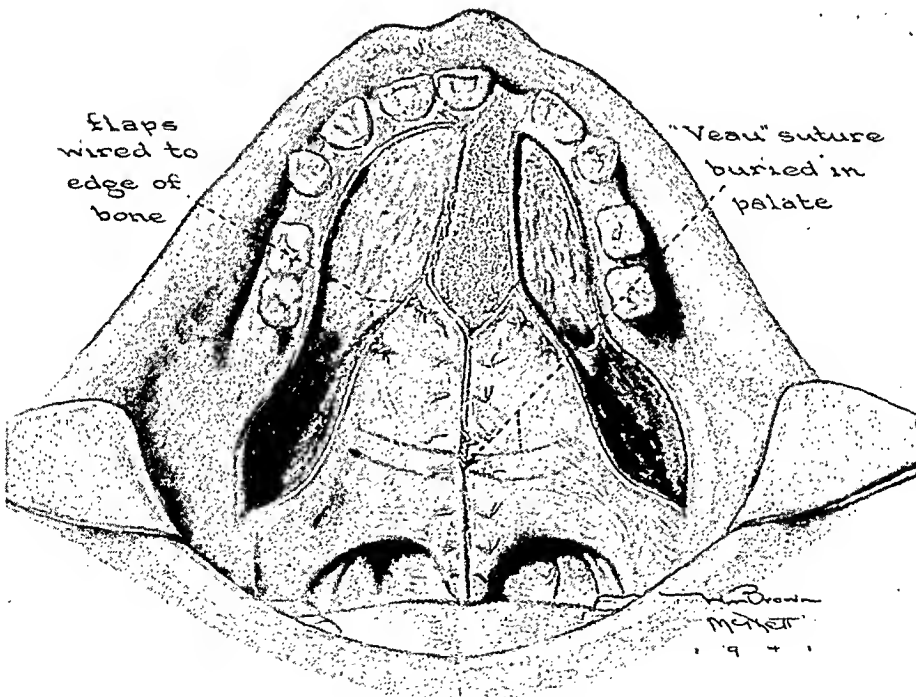
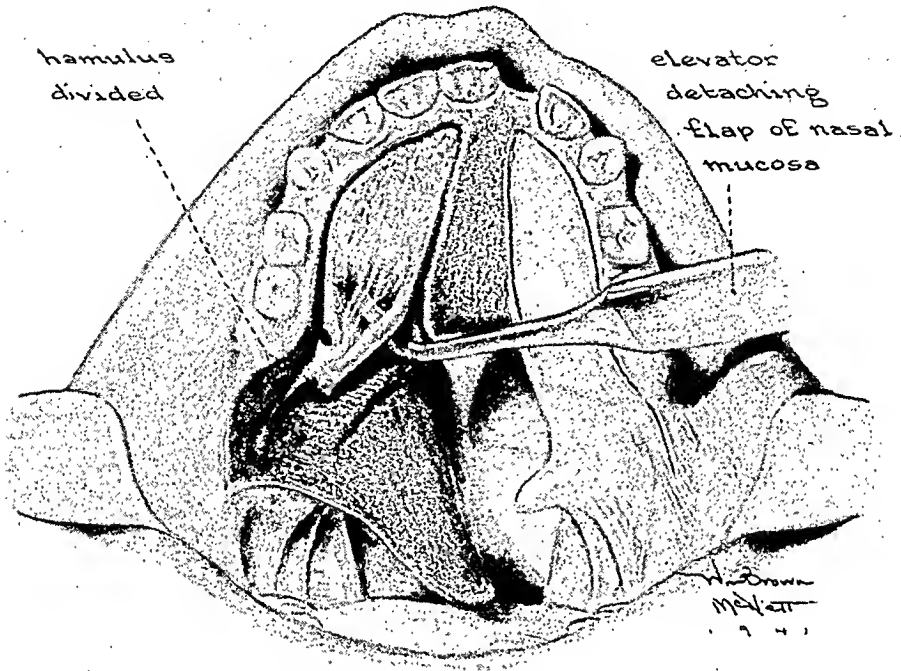


FIG. 26.

FIG. 25.—Elevation of flaps in preparation for skin graft in single lip-jaw palate cleft. Note how a portion of the nasal mucous membrane may be elevated.

FIG. 26.—Completed second stage of the "push-back" operation in single, complete lip-jaw palate cleft.

FIG. 27.

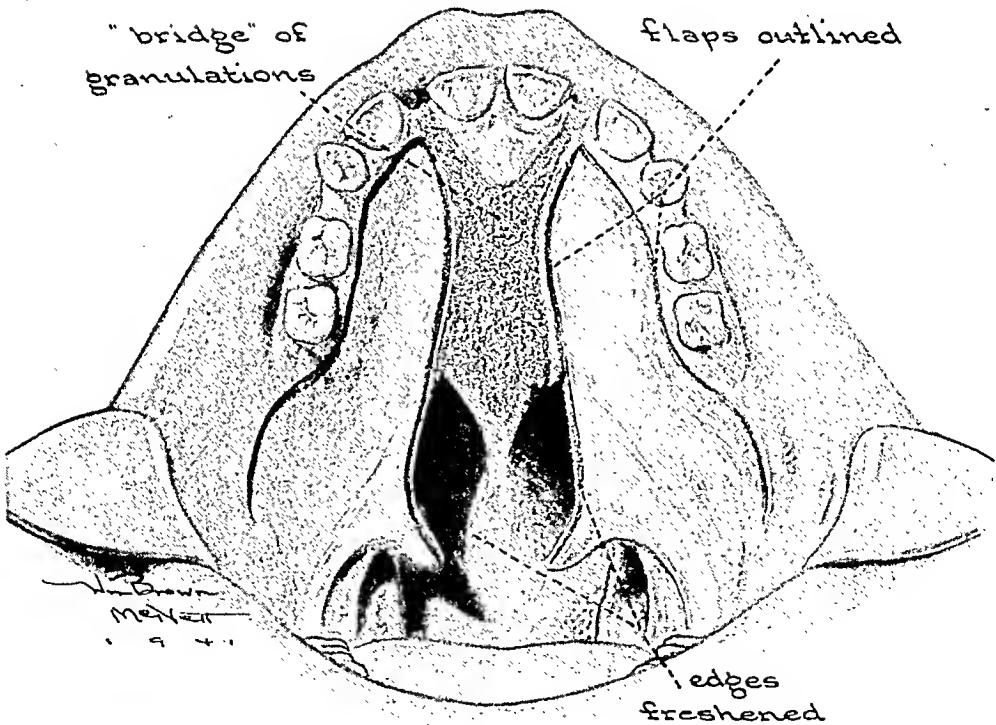
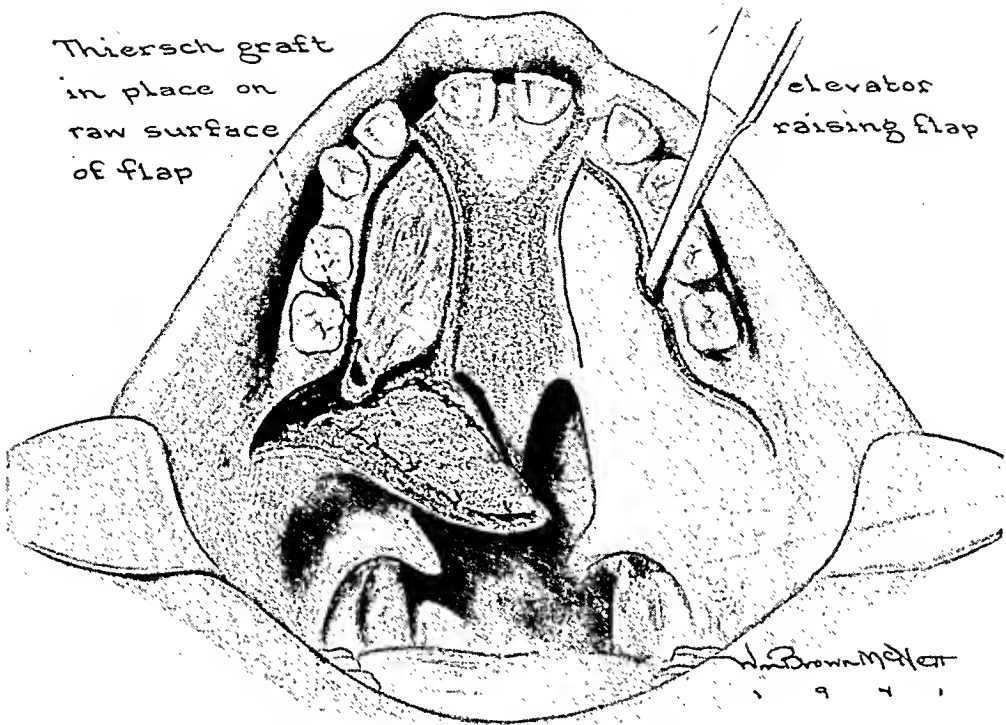


FIG. 28.

FIG. 27.—Raising of flaps and skin grafting in first stage of the "push-back" operation.

FIG. 28.—Incision for flaps in the final stages of the "push-back" operation.

one is often surprised to note that, in many cases, the vomer has developed to a point where the flaps may be utilized.

We are mindful of the additional stage-operation required, when the vomer flap technic is employed, but it so greatly simplifies the final or "push-back" operation that we feel it is indispensable. When the gauze is removed in ten days or two weeks, and the cavity has begun to fill in, it is smooth and rapidly blends with the contiguous surface of the palate (Fig. 27).

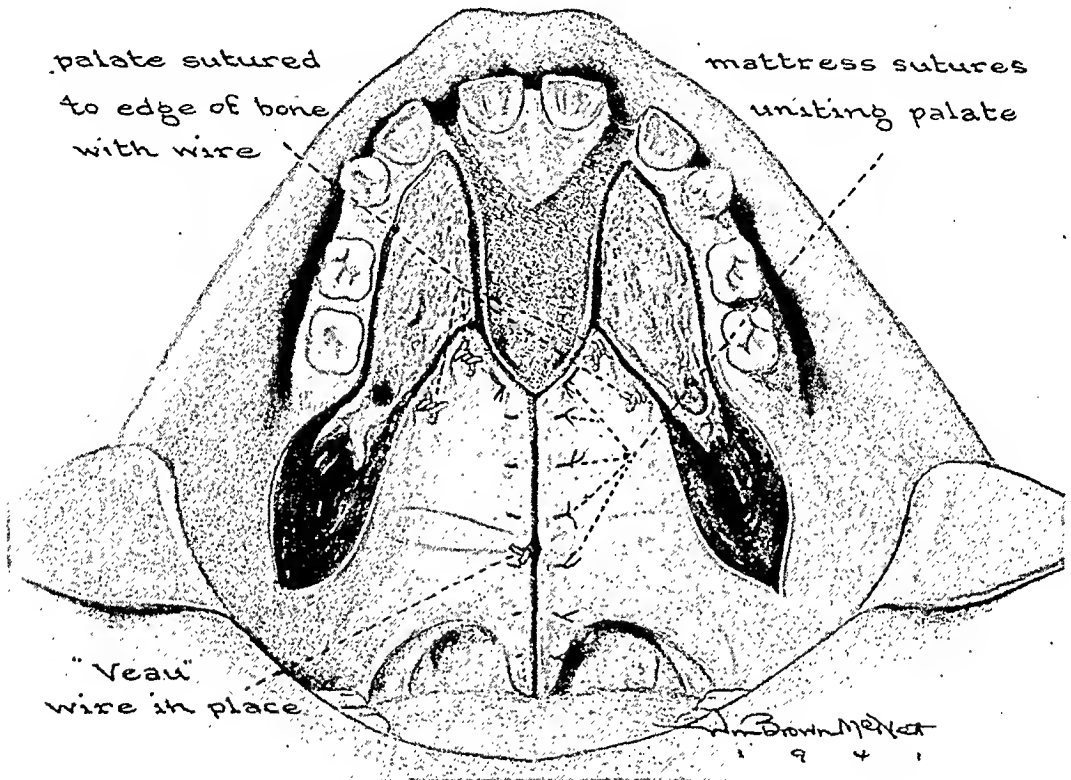


FIG. 29.—Demonstrating the completion of the final stage of the "push-back" operation in double cleft palate.

TYPE VI—COMPLETE BILATERAL CLEFT WITH RUDIMENTARY VOMER

The vomer is not available for use.

We have not been able to use Veau's method of pulling the nasal mucous membrane over for constructing a nasal lining in a large percentage of cases. In the high narrow arch, we have found it to be an impossibility. It may be accomplished in a low, wide vault, where the field of operation is much larger and the tissues are more accessible. Furthermore, when this procedure is employed, it is of value only when the Langenbeck, or similar operation, is performed for final correction. If further retrodisplacement is anticipated, the nasal mucous membrane will have to be supplemented. The skin graft, therefore, is the method of choice in these cases.

This is not intended as a criticism of Veau. On the contrary, we agree with him, as mentioned previously, that the necessity of a nasal lining is

axiomatic, but we feel that the use of the skin graft accomplishes this and permits the retrodisplacement necessary for a successful "push-back" operation.

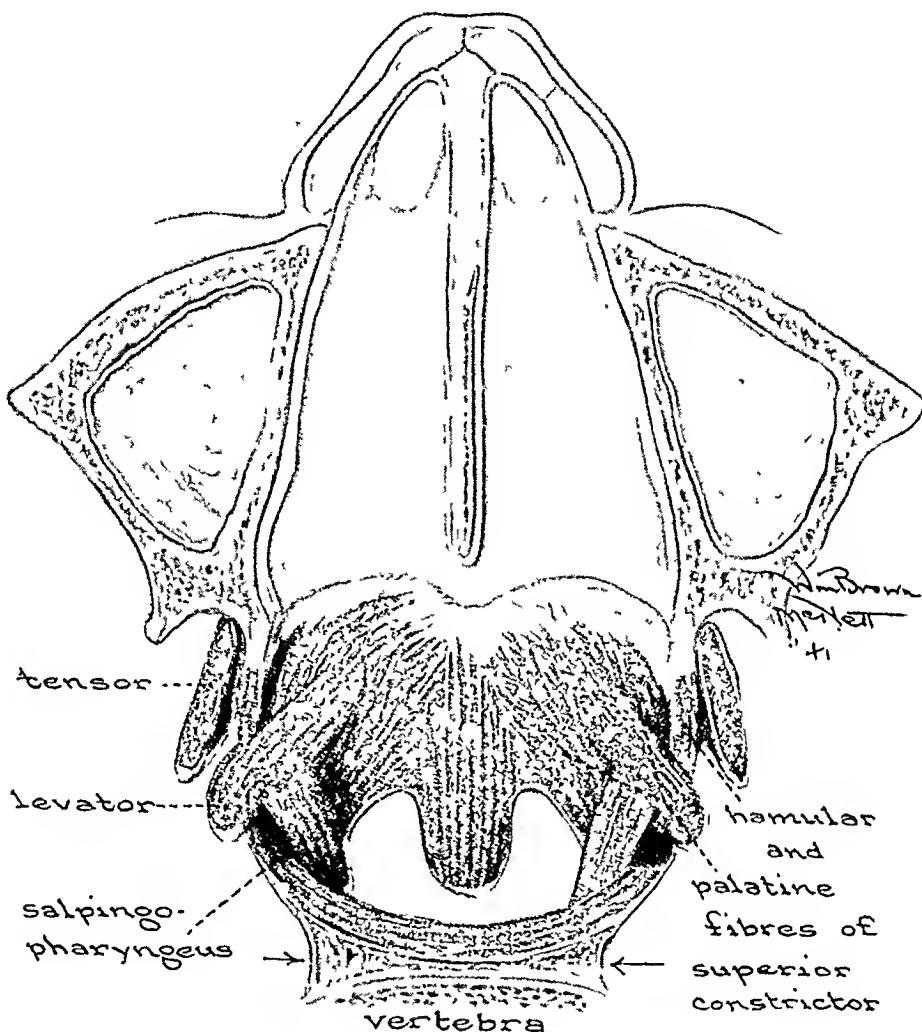


FIG. 30.—Demonstrating the position of the superior constrictor at rest. Note the palatine fibers of the superior constrictor which cause the shut-off.

SECONDARY REPAIRS

We have, in former papers, dwelt at length on the shortcomings of the mucoperiosteal and osteoplastic methods of cleft palate surgery. We feel, therefore, that mention of our methods of full correction of these previously operated cases is necessary. We classify these palates as operative successes but speech failures. We are mindful of the fact that the other surgeon's successes are not seen by us. We seldom see a palate which had been repaired by the Davies-Colley or Lane methods, where the tissues are in a state of sufficient vitality to risk further surgical correction. In the cases where we tried a "push-back" operation for correction of speech, little or no improvement resulted. We have twice successfully performed the "push-back" operation after a Brophy osteoplastic repair. We confess

that we have seen speech failures after a "push-back" operation. In such cases, the soft palate was not sufficiently separated from the hard palate structures to permit full retroposition. Many of our own Langenbeck repairs, performed years ago, have been functional failures.

The procedures for correcting these speech failures vary with the previous types and number of operations. Generally speaking, a modified

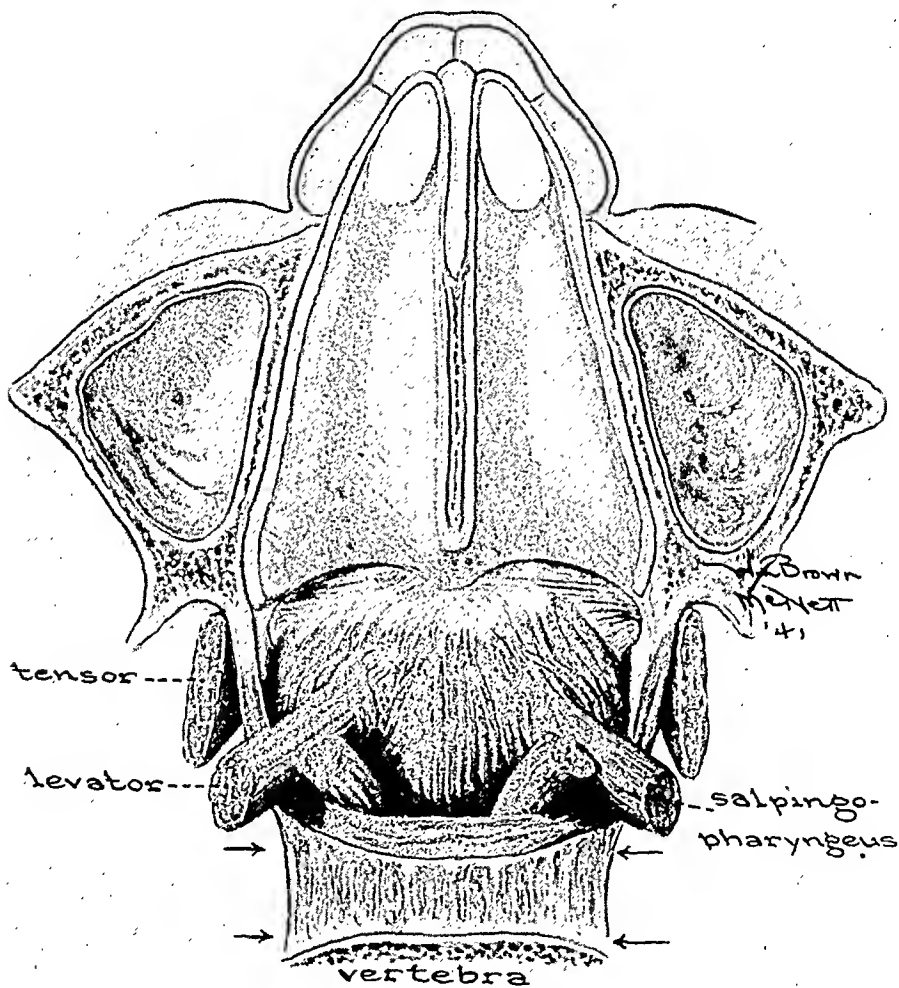


FIG. 31.—Demonstrating the position of the superior constrictor when contracted to produce the shut-off.

"push-back" forms the basis of correction on all patients who still have a palatal insufficiency and speak with the characteristic nasal tone. These secondary corrections have been very gratifying and all cases have been improved.

It is important to carefully plan the operation in each case so as to obtain maximum correction with minimum surgery. The plan is based on factors, the presence or absence of which influence the efficiency of the operation—the most important is the amount of bony palate present and the degree of vomer development.

Using a sharp needle, the edge of the bone is followed completely around the palate, automatically outlining the flaps.

The first stage consists of elevating the mucoperiosteum; dividing the palatine vessels (if not done at the previous operation). Next, insert the

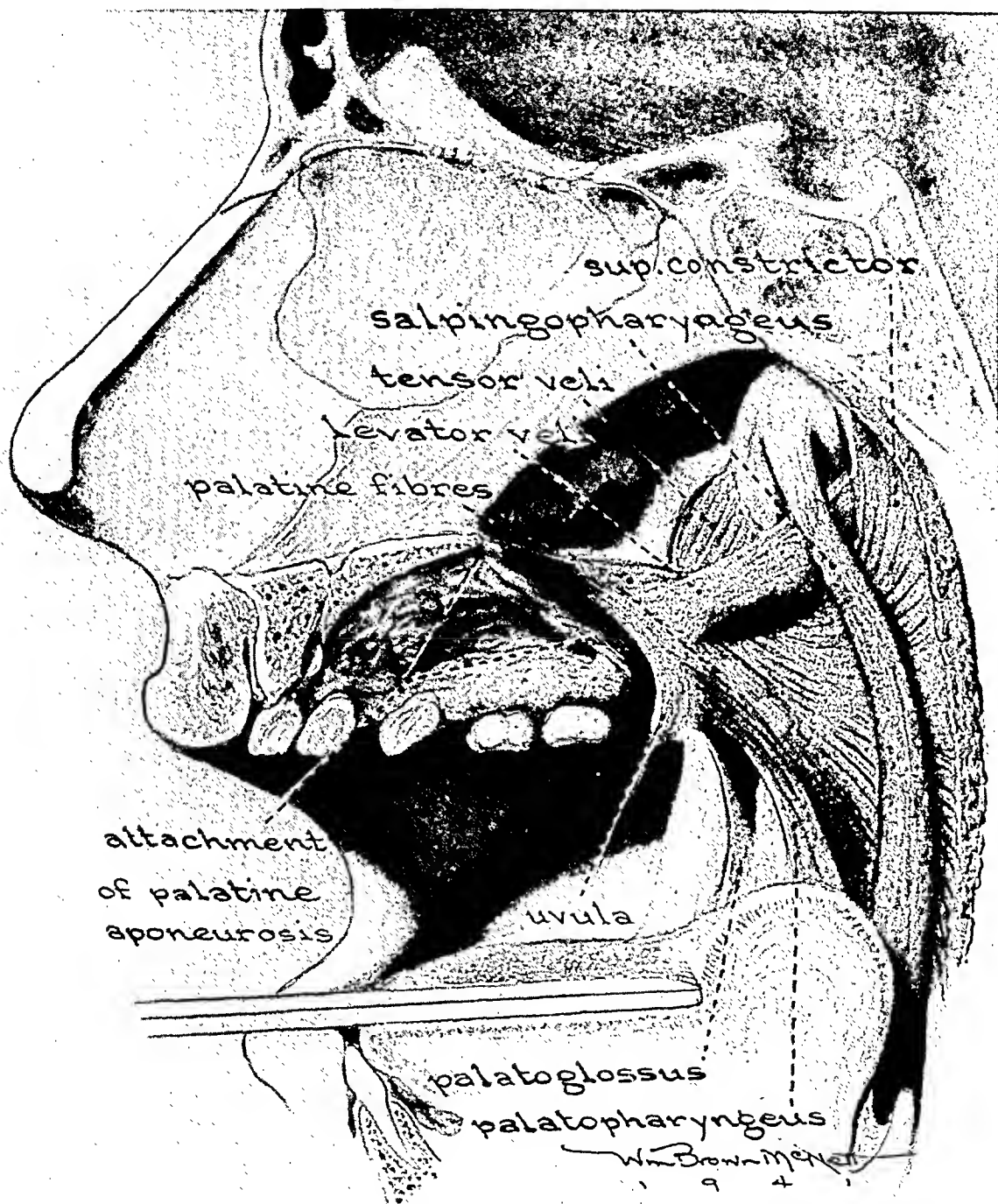


FIG. 32.—Lateral view of the position of the palate muscles in a cleft involving the bony palate, before operation.

skin graft if it is to be employed. It is very difficult to insert skin grafts in cases that have been operated upon many times before. Fortunately, the marked overproduction of fibrous tissue, existing from repeated trauma, is not so prone to contracture, and the skin grafts are not as necessary.

The second stage of the push-back operation is performed three to ten weeks later.

The hamular process is divided on each side, and the soft palatal tissues are completely separated from the posterior border of the hard palate. The lateral tissues are bluntly dissected out until the internal pterygoid muscle is reached, at which time there should be sufficient retroposition of

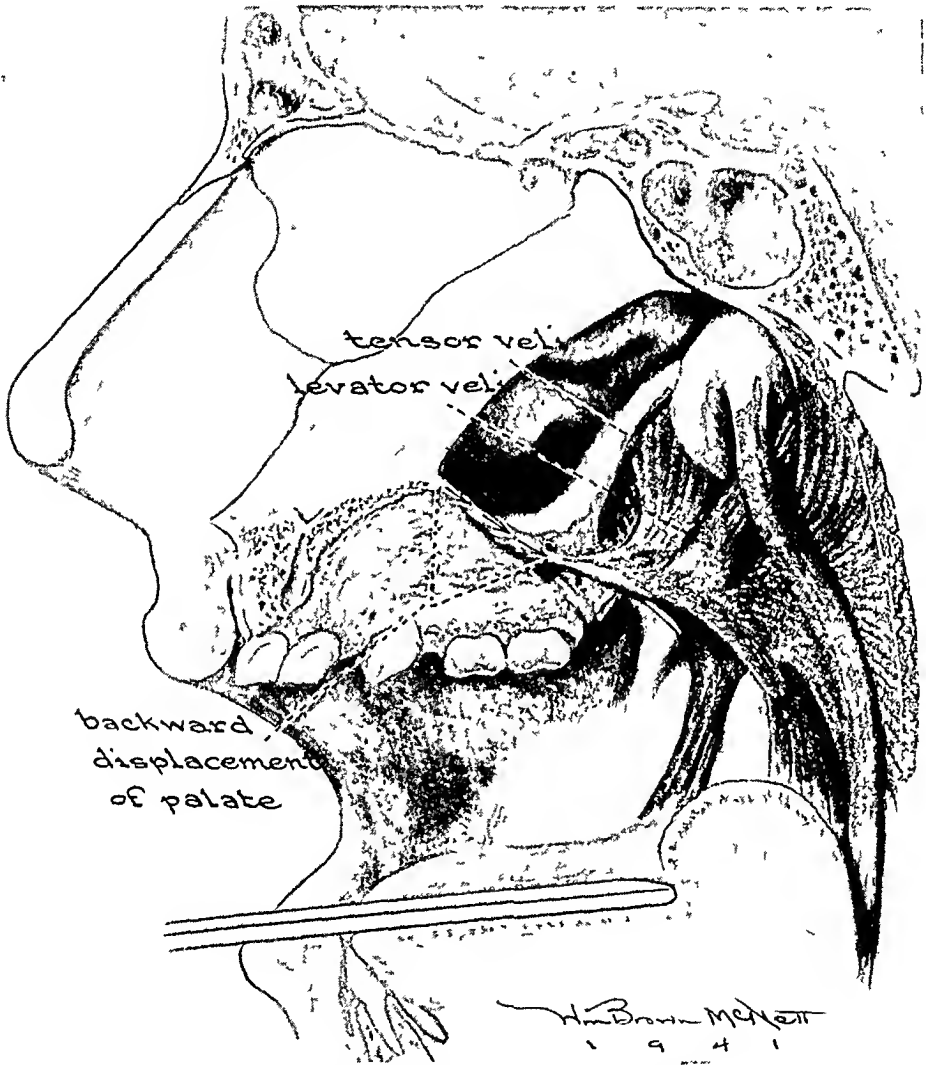


FIG. 33—Lateral view of the position of the palate muscles in a cleft involving the bony palate, after the "push back" operation

the tissues. The flap or flaps are then sutured as previously described in Figures 21-26.

It is to be emphasized that in these secondary repairs it is necessary that overcorrection be made.

SECONDARY PALATAL DEFECTS

All surgeons performing cleft palate operations have, at some time or other, been disappointed by having repeated failures in attempting to close secondary holes in the palate. The conventional operation, using lateral

relaxing incisions to allow flaps to close the defect, usually fails. The area above the repair forms a gutter for the accumulation of débris, and separation ensues. The presence of a mucous membrane-lining reduces the number of failures. The method of "turn-over," as advocated by Davies-Colley, has been disappointing. Illustrations of this method are very convincing, but successes in our hands have been few. Wherever possible, the mucous membrane is brought over, as shown by Veau. Unfortunately, the mucosa has not always been readily accessible. Our method of skin grafting, followed subsequently by lateral incisions and closure, has given more encouraging results.

CONCLUSIONS

Operations designed for the simple closure of a cleft palate are not adequate for producing articulate speech.

The "push-back" operation, in our hands, has increased the number of satisfactory speech results in cleft palate patients. This is particularly true in patients who have had previous operations, which resulted in but little speech improvement.

The surgical correction is based on findings, as a result of original investigation, and in the anatomy of the velopharyngeal mechanism.

The "push-back" operation establishes the normal muscle and palate position, so that proper velopharyngeal closure is made possible.

The use of vomer-flap transplant in cleft palate surgery has materially reduced the incidence of residual defects in the alveolar ridge. We feel that our modification of the method, by producing granulation with packing placed over the vomer flap, is essential if the "push-back" operation is employed.

The skin graft has produced a heavier flap of tissue, and minimized tissue contraction following palatal surgery. It has also given us a higher percentage of closure in correcting secondary palatal defects.

Nearly all cleft palates show some degree of bone deficiency, and while each type requires a different operation, our basis of all corrective surgery is the "push-back" operation, with variations for the individual case.

We do not advocate the use of pharyngoplasty as a routine procedure nor do we encourage posterior pillar surgery. Pharyngoplasty may be of great value in cases where the superior constrictor will not develop and produce Passavant's ridge or ring. There are cases that are surgically non-corrective because of insufficient tissue. The greatest gain in these cases is obtained by the use of an obturator. If, however, the "push-back" operation can be effected, even with a remaining defect in the anterior part of the palate, this is done, and the defect is covered with a small obturator.

THE MECHANISM OF SHOCK IN INTESTINAL STRANGULATION

AN EXPERIMENTAL STUDY

EVERETT IDRIS EVANS, M.D.*

BOSTON, MASS.

FROM THE SURGICAL LABORATORY OF THE HARVARD MEDICAL SCHOOL AT THE
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

FEW SURGICAL EMERGENCIES present a graver picture of shock than that seen in intestinal strangulation, especially if a long loop is involved, or the symptoms have persisted for several hours or more. The rapid, feeble pulse, the pale and often cold extremities, the low blood pressure, the anxious yet worn expression, all suggest a seriously decreased effective blood volume. When the peritoneal cavity is opened and the surgeon observes that the distended intestinal loops are bathed in thin, blood-tinged fluid, he is presented with direct evidence that the blood volume is reduced; but when the turgid, discolored loop is resected and opened to display the foul-smelling, blackened contents, it is difficult to resist the temptation to incriminate the loop contents (with their "toxins") as the most important, if not the sole initiating cause of the shock picture.

Experimental studies, too numerous to mention in detail, have been carried out for the purpose of determining the cause of death in closed intestinal loop obstruction. These, in the main, have served to focus attention on the extremely toxic nature of the contents of the closed loop (Whipple, Stone, *et al.*¹⁶). They have demonstrated that when cell-free extracts of the loop contents are injected *intravenously* into suitably prepared animals, the recipient animal becomes quite ill, shows signs of shock similar to that seen on histamine injection, and usually dies in profound collapse. Moon¹⁴ (1938) has indicated that these animals show pathologic changes similar to those seen in patients dying from shock, and has concluded that such studies provide strong evidence that shock can best be explained on the basis of generalized damage to all capillaries as a result of direct action of a toxin.

Few investigators interested in intestinal strangulation have paid close attention to the extent of plasma loss in this condition. There are two notable exceptions: Aird¹ (1937) placed a rubber bag around a loop of small bowel in cats, then strangulated the loop by tying a ligature around the neck of the bag tight enough to make the mesenteric pulsation just palpable. The blood loss was measured by comparing the weight of the bag plus the contained blood and intestinal loop with the same length of normal bowel. The results of nine experiments demonstrated that 50-80 per cent of the blood can be shunted from the effective circulation within 18-24 hours by this

* Rockefeller Foundation Fellow in Surgery. Assistant in Surgery, Medical College of Virginia, Richmond, Va.

method, and that the loss of blood varies directly with the length of loop strangulated.

Scott¹⁵ (1938), working in Wangensteen's laboratory, has published an excellent paper on the cause of death in intestinal strangulation. In an experimental study on dogs, in which various types of arterial and venous occlusion of the blood supply to loops of small intestine was produced by ligation, he found that in partial occlusion of arterial and venous systems the blood loss was 35 per cent; complete occlusion of blood supply, 22 per cent; complete occlusion of artery with patent vein, 20 per cent; and complete venous occlusion with patent artery, 55 per cent. Scott concluded that: "The loss of blood in strangulation obstruction has been calculated and found adequate, with the venous types of occlusion at least, to account for the shock and death which occur."

Gendel and Fine⁷ (1939), in their paper on plasma loss in intestinal obstruction, presented data on three dogs with a strangulated intestinal loop. By the dye method, these animals lost 30.8, 64.2 and 51.4 per cent of their blood volume during four hours of strangulation, respectively.

In our present studies on shock, we have been able to make a series of observations on plasma loss in intestinal strangulation, and to correlate this loss with the alteration in actual plasma volume of animals before and during the shock state. These are recorded below, with remarks on the relation of such data to the general problem of the initiating factors in shock.

Experimental.—The first few experiments demonstrated that if a small loop of the lower ileum was strangulated, the animals lived for 18 hours or more. Thereafter, the experiments were conducted in the following manner: Healthy dogs were used. After a 36-hour fast, the plasma volume was determined by the Gregersen⁹ dye method (1937) after the modification which employs the photo-electric colorimeter (Gibson and Evelyn,⁸ 1938). At this time, determinations of total plasma chlorides, nonprotein nitrogen, and hematocrit were made. That same evening, under evipal anesthesia adequate for a short celiotomy (usually 40–50 mg. per kilo), and with strict asepsis, a loop of lower ileum, 14 inches in length, the lower end of which was about six inches above the ileocecal valve, was ligated with a rubber band (5 Mm. in width). The ligature was drawn tightly enough to produce obvious obstruction to venous return from the loop of bowel, but only tightly enough to diminish slightly the arterial inflow. The intestines were returned to the peritoneal cavity, and the abdomen closed in layers, with silk sutures. By the time the skin was closed, the animals were usually coming out from the anesthesia, so the total anesthesia time was usually one-half hour or less. Evipal was employed as the anesthetic agent, rather than ether, first, because it probably does not affect the plasma volume as much as does ether (McAllister,¹² 1938, and Hamlin and Gregersen,¹⁰ 1938), and, secondly, because it gave the advantage of a very short anesthetic period. It is felt that the shock which subsequently developed could not have been influenced greatly by this procedure, in itself, and could not very plausibly be

attributed to the brief anesthesia. This should obviate the criticism of Moon¹⁴ (1938) that in certain experimental studies, the anesthetic may have been the cause of shock.

The next morning, 12–14 hours later, the animals were always in varying degrees of “shock.” The pulse was always rapid (150–220 per minute) with a weak pulsation in the peripheral arteries; the extremities were often cold; temperature (rectal) was usually elevated 1° – 2° C.; respirations were normal; more often than not, these animals could be induced to jump out of their cages. Only one dog was obviously moribund at this stage.

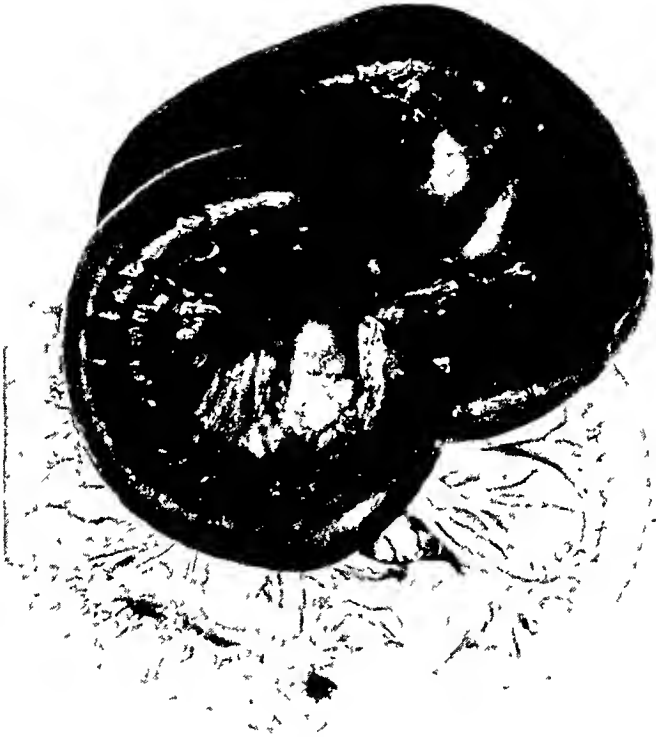


FIG. 1.—The appearance of a strangulated loop of bowel, contrasted with normal bowel after 14 hours of strangulation.

At this time, a second plasma volume determination was made, and, at the same time, the hematocrit, plasma protein, chlorides, and nonprotein nitrogen were determined. With local anesthesia, the blood pressure was measured with a mercury manometer from a cannula in the left femoral artery. The animals were then anesthetized with various anesthetic agents (these studies were reported in detail elsewhere [Evans and Beecher,⁴ 1941]); death ensued in 30 to 200 minutes. After death, the peritoneal cavity was opened carefully. The free blood-tinged fluid was collected with sponges, the amount and character recorded, and its protein content and hematocrit determined. A careful necropsy was then performed on each animal.

Necropsy Findings.—Figure 1 illustrates the usual appearance of the strangulated loop. The amount of free peritoneal fluid varied from 63 to 329 cc. The small bowel above the strangulated loop appeared normal.

sometimes being slightly distended with fluid. The stomach and duodenum were always normal in appearance. The spleen was always contracted; in three instances there were small hemorrhagic infarcts in this organ. The liver, lung, heart, kidneys, and adrenals were normal. In no instance did the lungs show evidence of edema, such as that described by Moon,¹⁴ (1938). In no instance was the pericardial lymph stained with the dye (T-1824) used in the determination of the second blood volume. This finding is in contradistinction to the findings of Freeman, *et al.*⁶ (1941), who induced "shock" by continuous adrenalin infusion. This has been discussed elsewhere in connection with the validity of the Gregersen dye method for plasma volume determination in the shock state (Evans and Hamlin,⁵ 1941). It may be stated here that in all but one experiment, the disappearance slope of the dye curve has been the same in the normal and in the shock state for the same dog.

As a final step, the strangulated loop was opened, its contents collected and measured. The loop contents were always dark red-black in color, possessed an extremely foul, permeating, sometimes nauseating odor, and resembled more closely laked whole blood, than plasma.

Experimental Observations.—I. In Table I are shown the chemical and physiologic data on these animals, in the normal state, and after 12–14 hours of intestinal strangulation. For brevity, representative data are shown for only 10 of the 29 dogs so studied.

TABLE I
CHEMICAL AND PHYSIOLOGIC DATA IN TEN ANIMAL EXPERIMENTS

Dog No.....	63	79	81	102	104	113	126	129	122	144
Weight.....	15.0	16.3	10.0	9.4	9.1	13.0	14.2	13.7	16.5	10.1
Hematocrit										
Before.....	47.0	38.0	34.0	41.0	41.5	42.8	44.2	46.8	43.6	58.3
After.....	53.0	48.5	42.5	58.3	50.8	48.7	53.2	48.9	61.5	65.0
Plasma Protein										
Before.....	5.35	6.63	5.97	6.31	6.33	5.85	6.35	5.42
After.....	5.29	6.60	5.87	6.07	5.48	6.32	5.70	5.66	6.52	6.31
Chlorides										
Before.....	106	101	110	106	128	120	120	120	116
After.....	108	103	102	98	120	132	108	124	116	120
Per Cent of Plasma Lost.....	—38	—25.3	—45.9	—34.8	—31.4	—23.4	—40.8	—27.1	—45.4	—35.2
CC. Plasma Lost, Dye Method	268	231	302	161	134	155	283	147	436	178
Fluid Collected										
Peritoneal Cavity.....	225	175	304*	148	119	158	155	98	329	160
Loop.....	50	10	152	65	174	48	82	95	50
Protein Content Peritoneal										
Fluid.....	4.21	4.46	4.80	6.89	4.56	8.30	4.77	5.04
Initial B. P. in Shock Mm. Hg	65	128	72	78	74	57	88	49	65	35
N. P. N.										
Before.....	20.0	30.0	26.4	30.0
After.....	36.4	42.2	44.5	69.0

*Total

It will be noted first that there has occurred during the experimental period a material decrease in actual circulating plasma, ranging from 25.3 to 45.9 per cent. The blood chlorides remain unchanged; this was to be expected because these animals do not vomit, so no gastric juice is lost. The hematocrit rises from 6.0 to 17.9 per cent; this hemoconcentration indicates a predominant loss of plasma rather than whole blood. The plasma protein

concentration is unchanged, indicating that if fluid is drawn from the extravascular spaces or tissues into the blood stream tissue proteins come with it. The nonprotein nitrogen rises very slightly; this may indicate a decrease in kidney function or perhaps the absorption of blood from the peritoneal cavity.

In Chart I, the initial blood pressure (after the 12-14-hour strangulation) is plotted against the decrease in plasma volume. It will be noted that the blood pressure appears to be fairly well maintained until the plasma loss

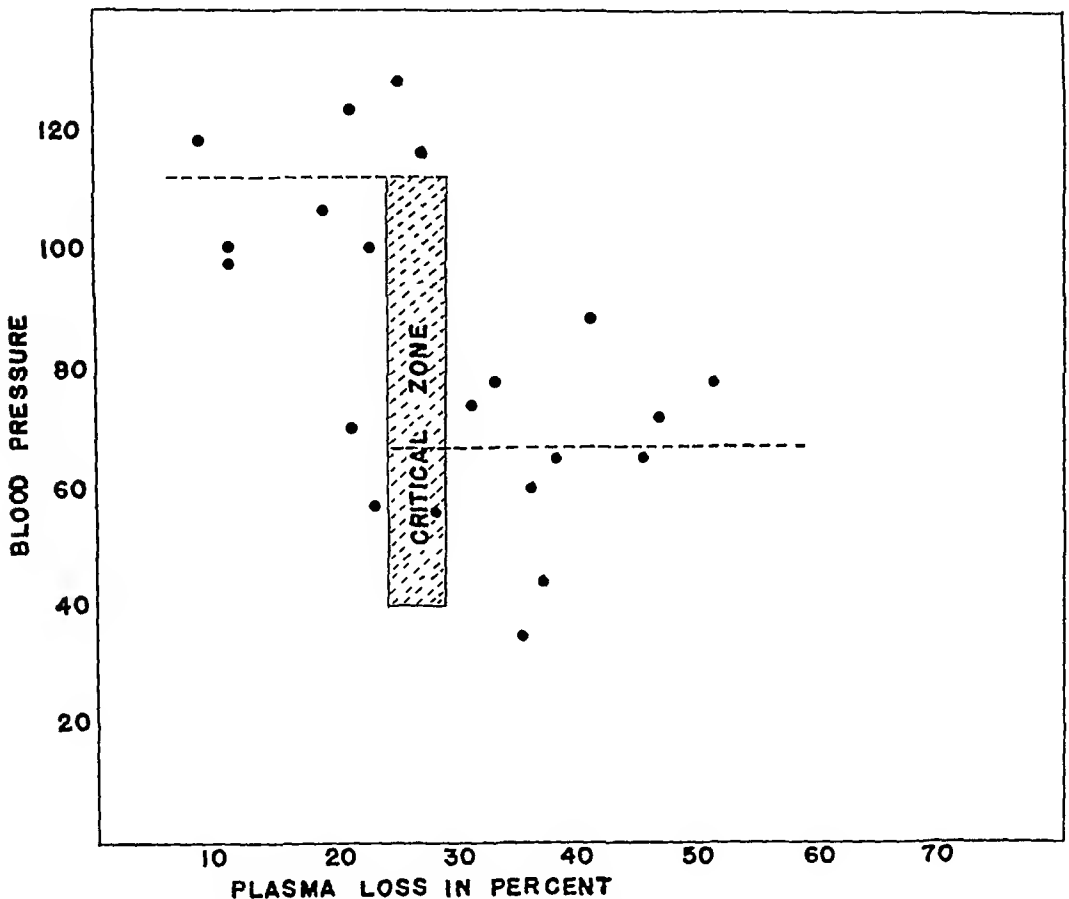


CHART I.—The apparent maintenance of blood pressure at normal levels until the plasma loss exceeds 25-28 per cent.

exceeds about 28 per cent. If a greater loss occurs, the blood pressure is obtained at "shock" levels.

An analysis of the data demonstrated that the pulse rate was always elevated, whether the plasma loss was in the neighborhood of 20 or 35 per cent. There appeared to be no close correlation between plasma loss and pulse rate.

THE RELATION OF THE VOLUME OF FREE PERITONEAL FLUID TO PLASMA LOSS

The free peritoneal fluid collected from these animals with strangulated loops had these characteristics: It was slightly pink to red in color, and contained varying numbers of red blood cells; when centrifugalized, the

hematocrit was low, 2.1 to 6.2 per cent. The supernatant fluid resembled the animal's plasma. If sodium thiocyanate had been injected (to determine extracellular fluid volume) the thiocyanate concentration of the animal's plasma was the same as that in the peritoneal fluid. The protein concentration was slightly lower than that in the plasma. The odor was that of the animal, never like that of the loop contents. If allowed to stand in a test tube for several minutes, a solid clot formed throughout the tube of free peritoneal fluid, just as in heparinized plasma to which has been added a sufficient amount of thrombin.

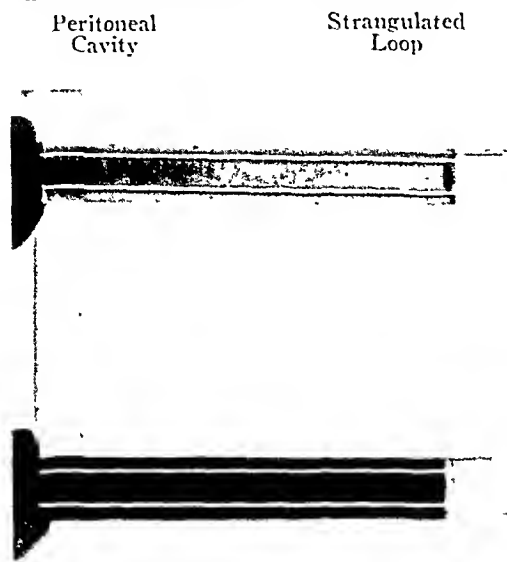


FIG. 2.—The centrifugalized free peritoneal fluid contrasted with that from the strangulated loop.

From these observations it has been concluded that the free peritoneal fluid in these shock animals closely approximates *plasma*. Figure 2 illustrates the centrifugalized free peritoneal fluid contrasted with the fluid from a strangulated loop.

In Table 1 and Chart 2 is presented a comparison between the amounts of free peritoneal fluid collected, (with its protein concentration), and the decrease in plasma volume as measured by the dye method. It will be observed that in most of the experiments practically enough free peritoneal fluid was collected to account for the plasma volume decrease.

When the volumes of the loop contents and free peritoneal fluid are considered together (Chart 2), it will be seen that the plasma seems to have been lost "locally," *i.e.*, in the loop or into the peritoneal cavity, rather than "generally" from the capillary bed of the entire body. The significance of this observation will be pointed out below.

THE TOXICITY OF THE FREE PERITONEAL FLUID

No one who has opened a strangulated loop of bowel could fail to have been impressed by the obvious toxic nature of the loop contents. The odor is so offensive, so fecal in character, that it is easy to imagine the serious consequences that must result should this material be absorbed unchanged into the blood stream. But there rests the problem: Do these substances in the strangulated loop get into the general circulation?

Absorption from the loop of bowel can take place only in three possible ways, namely, by the loop lymphatics, by the loop venous system, or by passage through the serous coat and then transperitoneally, to be absorbed either by the normal mesenteric vessels or by the lymphatics of the general peritoneal cavity.

In a strangulated loop, the venous and lymphatic return of the loop are obstructed; absorption can, therefore, take place only transperitoneally. If

this be true, then the only route by which toxic products in the strangulated loop can enter the general circulation is to pass through the serous coat of the strangulated bowel, into the fluid contents of the peritoneal cavity, and then into the general circulation *via* lymphatics or mesenteric circulation.

On this basis, the following experiments were carried out. Intestinal strangulation was produced in the described manner. When the dog was in quite severe shock, the free peritoneal fluid was collected under local

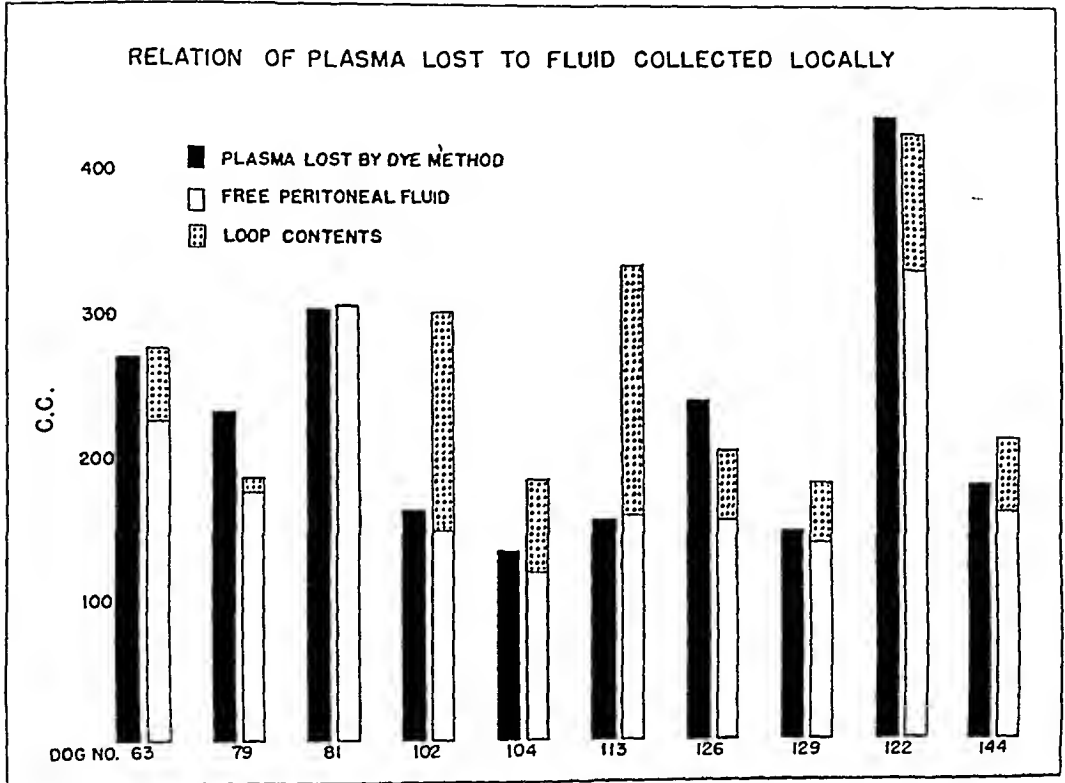


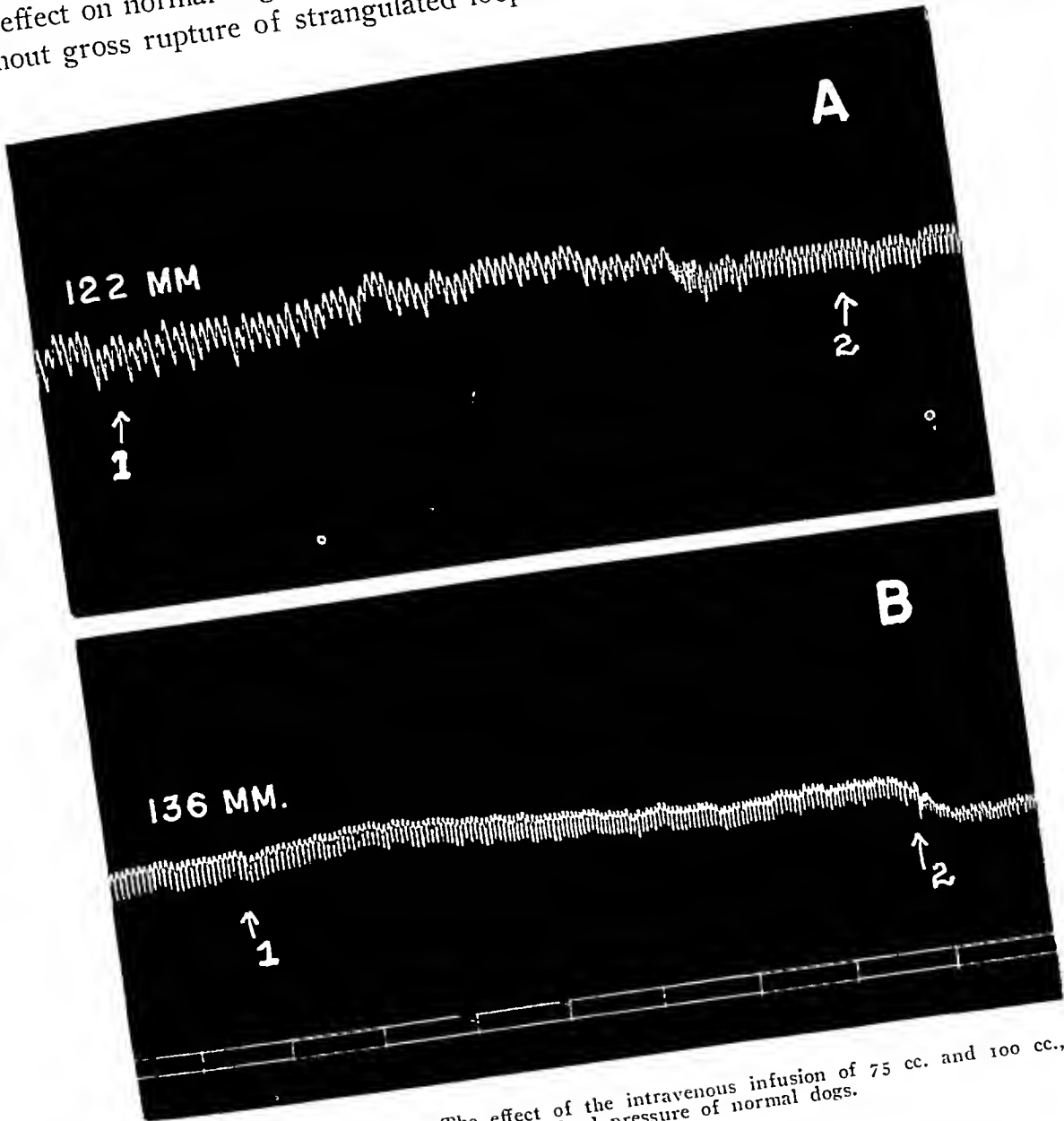
CHART 2.—The relation of plasma loss, as measured by dye methods, to fluid collected in the peritoneal cavity and in the strangulated loop.

anesthesia through a small incision in the abdominal wall, by aspiration and suction. Clotting was prevented by a small quantity of two per cent sodium citrate. About 100 cc. of peritoneal fluid was collected from each of three dogs in shock. This peritoneal fluid was then diluted with equal parts of 0.9 per cent NaCl solution and injected intravenously into suitable recipient animals. In Graph 1A is shown the kymographic tracing of the blood pressure curve, shortly before, during and after the intravenous infusion of 75 cc. of free peritoneal fluid taken from a shock dog. The response was a slight rise in blood pressure during the infusion. In Graph 1B is shown the kymographic tracing of the blood pressure curve of a normal dog under sodium amytal anesthesia, 50 mg. per kilo, during the intravenous infusion of 100 cc. of peritoneal fluid taken from another animal in shock. In none of three such experiments was there any evidence of the presence of a depressor substance in the free peritoneal fluid of these shock dogs. Dogs given such

INTESTINAL STRANGULATION

intravenous infusions appeared normal when they had recovered from the barbiturate anesthesia.

These findings corroborate those of Scott.¹⁵ He found that intravenous infusion of peritoneal fluid from dogs with intestinal strangulation was without effect on normal dogs if the peritoneal fluid came from animals that died without gross rupture of strangulated loops.



GRAPH 1.—A, and B. The effect of the intravenous infusion of 75 cc. and 100 cc., respectively, of peritoneal fluid on the blood pressure of normal dogs.

THE MECHANISM OF SHOCK IN INTESTINAL STRANGULATION

Discussion: In his treatise on traumatic shock, Blalock³ (1940) has emphasized that in an intelligent appraisal of the various possible causes of shock, one must take care to differentiate the *initiating* factors from the *sustaining* and *terminal* factors. This, many writers have failed to do, especially in statements about the cause of shock in intestinal strangulation. In the following paragraphs, there have been grouped together under the general headings of "initiating, sustaining, and terminal," the factors believed

to be important in the causation of shock in intestinal strangulation; they are thus separated because of their relation to the time-sequence during which they act. The sequence of events could be stated as follows:

A. *Initial Phase*: A loop of bowel is strangulated by torsion, a band, or caught by the neck of a sac (hernia). The venous flow is obstructed, while the arterial inflow is unimpaired. A high venous pressure develops locally in the strangulated loop, with increased capillary filtration *locally*, and when the endothelial capillary wall is damaged sufficiently, fluid and protein pour out into the lumen of the loop and through the serous coat into the free peritoneal cavity. Soon, practically pure plasma is passing through the capillary wall. The effective circulating plasma volume falls in direct ratio to the local loss of plasma, with a decreased effective blood volume (and diminished cardiac output) resulting if the condition persists.

B. *Sustaining Phase*: The blood pressure remains elevated as long as the plasma loss can be compensated for by the protective vasoconstrictor mechanism. There is still only local damage, *i.e.*, in the affected loop. When the plasma loss exceeds a certain value, *e.g.*, above approximately 25–30 per cent, the vasoconstrictor mechanism ceases to be effective because of a marked disparity between the effective blood volume and the size of the vascular bed. The blood pressure falls, and the cardiac output diminishes. If this state persists for long, the blood flow to all tissues diminishes to such an extent that *generalized* increased capillary permeability may develop.

C. *Terminal Phase*: Generalized capillary damage is attended by rapid leakage of protein and fluid from the vascular bed to the extracellular and lymph spaces; hence pulmonary edema, capillary stasis, necrosis of bowel mucosa, *etc.* During this phase, the bowel wall of the strangulated loop may be so damaged as to become permeable to any of the contents of the loop, and they pass into the peritoneal cavity; a general toxemia develops, with death ensuing.

Such data as have been gathered in the present study seem to fit well into this conceptual scheme. We know that the venous strangulation of an intestinal loop early results in local damage, with plasma loss, because that can be easily observed when the animal is still under anesthesia. At the end of 12–14 hours it can readily be demonstrated that there is a *local* loss of plasma because plasma-like fluid can be collected from the peritoneal cavity. This fluid closely resembles plasma; the extent of the plasma loss as estimated by dye methods can be readily accounted for by the amount of plasma collected “locally” (Chart 2). It, therefore, seems quite unnecessary, and somewhat illogical, to attempt to account for this plasma loss by invoking a “generalized” loss of plasma, in the initiating, and, probably, sustaining phases of shock.

The relative absence, so far as could be demonstrated by depressor response when given *intravenously*, of any “toxins” in the free peritoneal fluid of these shock dogs is presumptive evidence that in the initiating phase of this type of shock “toxins” are not important causative factors. I have

not the slightest doubt that the loop contents are extremely toxic, especially when administered intravenously or intraperitoneally. As pointed out by Gatch and Culbertson¹⁷ (1935), however, "the crucial test (of the intoxication theory) must be the demonstration that toxic material is actually absorbed from the obstructed bowel." If it be admitted that in strangulated loop experiments the only absorption of such "toxins" is transperitoneally, it would seem, in the light of the above evidence, that this "demonstration" is still lacking.

The pathologic findings in the present group of shock dogs are decidedly different from those described by Moon and Morgan¹³ (1936) with a similar shock preparation. However, in their experiments, in which evidence of generalized capillary damage was found (pulmonary edema, bowel mucosal hemorrhage, *etc.*), the animals were allowed to *die* from shock. These changes would be expected in animals dead from shock, if the "sustaining" and "terminal" phases were long enough to permit generalized capillary damage.

Although Moon and Morgan injected strangulated loop contents, and found them extremely toxic, enough so to produce death when injected *intravenously*, they did not test the toxicity of the free peritoneal fluid of their shock animals, even though they agree that when the blood and lymph channels of a strangulated loop are obstructed, absorption of toxic products must take place "in part by diffusion into the peritoneal cavity with absorption through the peritoneal surfaces."

An abundance of data on plasma and blood loss in experimental traumatic shock has led both Blalock and Phemister to the conclusion that most of the blood or plasma loss is "local" at the site of injury, and that there is only a minimal loss of plasma through indirectly damaged capillaries or into areas of capillary stasis remote from the site of injury ("traumatic toxemia"). Blalock² (1931) states "the observations thus far indicate that the local loss of fluid at the site of injury is the most important factor in producing the decline in blood volume and blood pressure in shock. Evidence was not found for the action of toxins in these experiments."

It would appear from the experiments recorded here that substantially the same view might be taken for the cause of shock in intestinal strangulation; that the local loss of fluid from the strangulated loop of intestine is the most important factor in producing the fall in blood volume and blood pressure. No evidence for the action of toxins was found in these experiments.

CONCLUSIONS

In an experimental study of shock produced by strangulation of a short loop of ileum, it has been found that there occurs a large loss of plasma *locally*, great enough in itself to account for the fall in blood volume and blood pressure. There was no evidence found for plasma loss from capillaries damaged by "toxins," remote from the site of injury.

It is a pleasure to acknowledge my indebtedness to Dr. E. D. Churchill, who intro-

duced me to his concepts of the shock problem, and to Dr. Henry K. Beecher, for the facilities of his laboratory.

BIBLIOGRAPHY

- ¹ Aird, I.: *Edinburgh Med. J.*, **44**, 28, 1937.
- ² Blalock, A., Beard, J. W., and Johnson, G. S.: *J. A. M. A.*, **97**, 1794, 1931.
- ³ Blalock, A.: *Principles of Surgical Care*. C. V. Mosby Co., St. Louis, Mo., 1940.
- ⁴ Evans, E. I., and Beecher, H. K.: In preparation.
- ⁵ Evans, E. I., and Hamlin, E.: In preparation.
- ⁶ Freeman, N., Freedman, H., and Miller, C. C.: *Am. J. Physiol.*, **131**, 545, 1941.
- ⁷ Gendel, S., and Fine, J.: *ANNALS OF SURGERY*, **110**, 25, 1939.
- ⁸ Gibson, J. G., Jr., and Evelyn, K. A.: *J. Clin. Invest.*, **17**, 153, 1938.
- ⁹ Gregersen, M. I., and Gibson, J. G., Jr.: *Am. J. Physiol.*, **120**, 494, 1937.
- ¹⁰ Hamlin, E., and Gregersen, M. I.: *Am. J. Physiol.*, **125**, 713, 1939.
- ¹¹ Hill, J. M., Muirhead, E. E., Ashworth, C. T., and Tiggert, W. D.: *J. A. M. A.*, **116**, 395, 1941.
- ¹² McAllister, F. F.: *Am. J. Physiol.*, **124**, 391, 1938.
- ¹³ Moon, V. H., and Morgan, D. R.: *Arch. Surg.*, **32**, 776, 1936.
- ¹⁴ Moon, V. H.: *Shock and Related Capillary Phenomena*. Oxford Univ. Press, New York, 1938.
- ¹⁵ Scott, H. G.: *Arch. of Surg.*, **36**, 816, 1938.
- ¹⁶ Whipple, G. H., Stone, H. G., and Berneheim, B. M.: *J. Exp. Med.*, **17**, 286, 323, 1913.
- ¹⁷ Gatch, W. D., and Culbertson, C. G.: *ANNALS OF SURGERY*, **102**, 619, 1935.

FLUID, PROTEIN AND ELECTROLYTE ALTERATIONS IN EXPERIMENTAL INTESTINAL OBSTRUCTION*

W. E. ABBOTT, M.D., R. C. MELLORS, Ph.D., AND E. MUNTWYLER, Ph.D.

CLEVELAND, OHIO

FROM THE DEPARTMENTS OF SURGERY AND BIOCHEMISTRY, WESTERN RESERVE UNIVERSITY
SCHOOL OF MEDICINE, CLEVELAND, OHIO.

IN 1928, FOSTER,¹ in clarifying the status of acute intestinal obstruction from an experimental and clinical point of view, chose to define two arbitrary entities: (1) Acute simple obstruction of the continuity of the gastro-intestinal tract without primary vascular derangement; and (2) acute intestinal strangulation with interference to the vascular supply of the part. Thus, simple constrictions or bands about the intestine produce acute simple obstruction without vascular derangement, provided that the degree of distention of the occluded bowel is not excessive. Herniation or volvulus of a loop of intestine produces in addition to the obstruction a disturbance of its vascular tree. The multiplicity of factors that may enter into the pathogenesis of intestinal obstruction makes it imperative that each experimenter carefully assess the rôle played by the several physiologic and pathologic processes involved. For example, it is important to have information concerning the extent of the following: The plasma and interstitial volume dehydration; the disturbance of the acid-base equilibrium; the distention and ischemia of the preoccluded bowel; the vascular derangement associated with strangulation, as well as to keep in mind the regional differences in function (secretory, absorptive) and adaptability of different levels of the gastro-intestinal tract.

The present study was undertaken to evaluate, quantitatively, the changes in the plasma (T-1824) volume and the "available (thiocyanate) fluid," or roughly the extracellular fluid volume in dogs with pyloric, jejunal, terminal ileal, and colonic obstruction; to interpret, on the basis of these changes, the reliability of the hematocrit and plasma protein concentrations as indices of plasma dehydration; and to consider the rôle of certain factors in influencing the rate of development of dehydration and the severity of the symptoms in experimental obstruction.

METHODS

The obstruction of the gastro-intestinal tract of dogs was produced, under anesthesia, by tying a surgical tape one centimeter in width about the desired portion in such a manner as to occlude the lumen and yet not to produce ischemic necrosis and perforation. The degree of interference with the vascular supply in such a preparation depends subsequently upon the magnitude of the distention of the intestine proximal to the obstruction. In

* Aided by a grant from the John and Mary R. Markle Foundation.

some animals, as judged by the clinical course and the postmortem gross and histologic examination, the interference with the vascular supply to the part was minimal; in others, with great distention of the preoccluded portion, the rôle of a decrease in circulation to the segment was more prominent.

The time required for operation and anesthesia was short (15 to 30 minutes) and the degree of dehydration produced was minimal (as indicated by changes in the hematocrit and plasma protein concentration). In some cases before the abdomen was closed, physiologic saline was given intraperitoneally to combat dehydration due solely to the operative procedure. In order either to induce or to minimize a rapid loss of body water by emesis, water and food were either given or withheld from the animals in the postoperative period.

Fasting blood samples were carefully collected with greased syringes to avoid hemolysis. The plasma (T-1824) volume and the "available (thiocyanate) fluid" volume (or roughly the extracellular fluid volume) were determined by the direct method of Gregersen and Stewart² as modified for the photo-electric colorimeter by Gibson and Evelyn.³ The hematocrit determinations were made with heparinized blood in Sanford-Magath or Van Allen tubes, the plasma protein determinations were made by the micro-Kjeldahl technic and the falling-drop method of Barbour and Hamilton,⁴ and the plasma chloride determinations by the method of Van Slyke,⁵ as modified by Wilson and Ball.⁶ The total amount of circulating plasma protein was obtained by multiplying the plasma volume by the plasma protein concentration in grams per cubic centimeter. The percentage changes of the plasma volume, thiocyanate volume, and total circulating proteins were based upon individual control levels. At death, a gross pathologic examination was made, and sections of the viscera were taken for microscopic study.

RESULTS OF EXPERIMENTS

Pyloric obstruction was produced in eight dogs. The findings are shown in Table I. It can be seen that the hematocrit and plasma protein concentration showed a progressive rise in every instance except in Dog C-6 and Dog 360. In the former the hematocrit rose initially and then stabilized at about 45 in the presence of a progressive dehydration (as indicated by the plasma volume studies) and in the absence of hemorrhage. In Dog 360 the hematocrit fell terminally after an initial rise. In this dog and in Dog 359 gross and microscopic pathologic changes characteristic of shock were present.

All of these animals were permitted to eat and drink, and the magnitude of the loss of body water was found to parallel fairly well the amount and frequency of vomiting. The plasma volume after one to three days of obstruction showed a decrease varying from 9 to 46 per cent and the "available (thiocyanate) volume," or roughly the extracellular fluid volume, showed a loss varying between 5 and 30 per cent.

INTESTINAL OBSTRUCTION

TABLE I
BLOOD STUDIES OF DOGS WITH PYLORIC OBSTRUCTION

Dog No.	Postoper. Day	Hematocrit Cc./100 Cc.	Plasma Chlorides M. Eq./L.	Plasma Protein Gm./100 Cc.	Plasma Volume in Cc.	Percentage Change of Volume Plasma Thiocyanate		Percentage Change in Total Circulating Plasma Protein
C-1*	0	42.6	115.5	5.75	600			
	1	48.7		7.86				
	2	51.4	98.5	9.25	417	-30	-28	+12
C-2*	0	49.7	109.1	5.78	836			
	2	59.1	88.1	8.70	450	-46	-21	-19
C-3*	0	40.8	112.0	8.20	868			
	1	45.2	97.0	9.45	692	-20	-10	-8
C-4*	0	38.0	114.1	6.24	591			
	1	44.2		7.30	538	-9	-15	+7
	2	45.6	113.3	8.03	539	-9	-8	+17
C-5*	0	47.5	111.2	6.63	935			
	1	50.8	101.3	6.92	785	-16	-5	-12
	2	51.8	97.2	7.97	745	-25	-6	-4
C-6*	0	42.4		6.86	1148			
	1 1/3	44.6		7.64				
	1	45.3		8.02	866	-25	-7	-12
	2	45.2	87.9	8.71				
	3	45.3	73.6	9.23	760	-34	-11	-11
359†	0	33.2	111.2	6.43	865			
	1	46.0	103.6	7.33				
	2	50.7	99.0	8.81	630	-27	-30	0
360†	0	49.4	112.0	6.80	637			
	1 1/2	57.5	106.7	7.78				
	1	65.0	102.3	9.36	498	-22	-25	+7
	1 1/2	61.5	105.7	9.50				

*Dog killed. Autopsy showed no pathologic evidence of shock.

†Dog allowed to go on to death. Autopsy showed pathologic changes characteristic of shock.

Although the hematocrit and plasma protein concentration indicated dehydration, they did not reflect the actual loss of the plasma volume. The electrolyte loss as indicated by the chloride level in this series varied widely, but could be correlated quite well with the extent of vomiting.

TABLE II
BLOOD STUDIES OF DOGS WITH JEJUNAL OBSTRUCTION

Dog No.	Postoper. Day	Hematocrit Cc./100 Cc.	Plasma Chloride M. Eq./L.	Plasma Protein Gm./100 Cc.	Plasma Volume in Cc.	Percentage Change of Volume Plasma Thiocyanate		Percentage Change in Total Circulating Plasma Protein	Remarks
316	0	43.5	110.0	5.94	565				Food and water permitted. Obstruction released after 3 days. I. V. norm. saline given (750 cc. x 2).
	1	55.8	98.1	7.78					
	2	57.0	80.1	8.40	431	-24	-16	+8	
	5	41.2	96.7	5.67	538	-5	+1	-10	
	40	41.5	108.6	6.46	570	+1	0	+9	
42-9*	0	46.0	108.4	5.95	835				Dog took very little food and water. Died 30 hours after last studies.
	3	63.0	107.1	8.71	578	-31	-30	+1	
	4	61.6	108.1	8.02	795	-5	-19	+29	
	5	63.2	110.7	7.93	710	-15	-23	+13	

*Dog allowed to go on to death. Autopsy showed pathologic changes characteristic of shock.

In Table II the findings on two dogs with high jejunal obstruction are shown. They reacted much like the dogs with pyloric obstruction, and here the rapidity of dehydration again depended largely on the amount of vom-

iting. In Dog 316 physiologic saline was given and the obstruction was released after three days, and the animal eventually showed a return to normal.

TABLE III
BLOOD STUDIES OF DEHYDRATED DOGS WITH ILEAL OBSTRUCTION

Dog No.	Postoper. Day	Hemato- crit Cc./100	Plasma Chloride M. Eq./L.	Plasma Protein Gm./100	Plasma Volume in Cc.	Percentage Change of Volume			Percentage Total Change in Circulat- ing Plasma Protein	Remarks
						Plasma	Thio- cyanate			
316 [†]	0	41.5	108.6	6.46	570					Food and water per- mitted but largely re- fused after 3 days. Low ileal obstruction.
	3	46.7	99.9	7.83	532	- 7	-15	+13		
	6	41.7	96.6	7.04	539	- 5	-22	+ 3		
	9	39.7	95.9	6.90	482	-15	-22	-10		
	12	35.9	97.0	6.61	473	-17	-23	-15		
319 [†]	0	37.6	110.8	5.62	655					Given 500 cc. saline after blood studies on 3d day. Low ileal obstr.
	3	44.1	107.0	6.38						
	4	35.2	106.6	5.69	495	-25	-15	-23		
337 [†]	0	44.5		6.29	637					Very little food and water permitted. High ileal obstruction.
	2	47.5	101.4	7.11						
	3	16.4	91.6	6.71	583	- 9	-15	- 2		
	4	46.1	91.9	6.92	502	-21		-13		
338 [†]	0	16.2	112.6	5.83	850					Very little food and water permitted. High ileal obstruction.
	2	47.6	107.6	6.09	670	-21	- 8	- 8		
	4	46.1	111.7	6.02	648	-24	-16	-13		
339 [†]	0	60.0	109.2	6.03	870					Food and water per- mitted. Midileal ob- struction.
	3	63.2	85.0	7.65	432	-50	-18	-37		
	3 1/2	67.1	78.8	8.85						
42-10 [†]	0	55.5	105.2	5.70	749					No food and water. Low ileal obstruction.
	2	57.0	113.4	7.05	698	- 7	- 2	+15		
	5	58.0	111.5	7.86	655	-13	-12	+21		
	2	34.4	113.4	5.97	657	-33	-24			
42-13 [†]	1	35.7	115.6	6.55	705	-28	-27			Given no food and very little water. Dog con- sumed own vomitus.
	7	40.4	122.0	7.14	674	-31	-33			
	10	41.6	123.9	7.89	599	-39	-36			

[†]Dog killed. Autopsy showed no pathologic evidence of shock.

[Dog allowed to go on to death. Autopsy showed pathologic changes of shock.

In Table III the results are shown in seven dogs with ileal obstruction. In most instances the experimental value for the hematocrit and plasma protein concentration indicated directional changes in the plasma volume when compared with the control levels, but rarely did they indicate quantitative changes. The plasma volume again varied widely (-7 to -50 per cent) depending on the amount of food and water consumed and, thus, the associated vomiting. The plasma chloride concentration in Dogs 337 and 339 was low because of extensive vomiting and normal or high in Dogs 338, 42-10 and 42-13 in which practically no vomiting occurred. The decrease in the total circulating plasma proteins was often great, although in no instance was this discernible from the plasma protein concentration. In Dogs 316 and 42-13 vomiting was infrequent and there was little evidence of distention. In such animals, as the survival period was more prolonged, the hematocrit and plasma protein concentration were even less reliable indices of the extent of dehydration because of the effect of malnutrition.

The findings in animals with colonic obstruction are presented in Table

INTESTINAL OBSTRUCTION

TABLE IV
BLOOD STUDIES OF DOGS WITH COLONIC OBSTRUCTION

Dog No.	Postoper. Day	Hemato-		Plasma		Percentage		Percentage		Total	Remarks
		Cc./100	Chloride	Gm./100	Volume	Change of	Volume	Thio-	Circulat-		
		Cc.	M. Eq./L.	Cc.	in Cc.	Plasma	cyanate	Protein	ing Plasma		
333*	0	48.7	106.0	6.66	785						Food and water per- mitted.
	3	50.2	97.9	7.38	750	- 4	0	+ 6			
344*	0	47.2	113.3	5.92	607						Food and water per- mitted. Vomiting not marked.
	3	45.9	105.3	5.58							
	5	43.2	103.1	5.41							
	8	44.3	97.4	5.66	583	- 4	- 9	- 8			
	11	40.8	94.3	5.31	526	-13	- 7	-22			
	12	45.1	102.0	5.58							
345†	0	51.6	103.6	6.76	812						Food and water per- mitted. Vomited last 6 days and refused feedings.
	2	53.3	98.4	6.73							
	5	50.7	97.2	6.40							
	8	54.2	87.5	6.53	640	-21	-13	-24			
	10	53.0	81.6	6.49	618	-24	- 8	-27			
	13	52.5	80.9	8.04	445	-45	-27	-35			
42-7†	0	47.6	105.2	6.58	600						Dog permitted food and water.
	3	51.0	97.4	7.32	578	- 4	0	+ 7			
	7	50.0	93.7	6.21	568	- 5	-12	-12			
	10	53.8	86.8	6.03	558	- 7	-12	-15			
	14	55.2	77.5	5.37	392	-35	-15	-47			

*Dog killed. Autopsy showed no pathologic evidence of shock.

†Dog allowed to go on to death. Autopsy showed pathologic changes characteristic of shock.

IV. In this series it can be seen that the hematocrit and plasma protein concentration are not reliable indices of the plasma volume change owing largely to the effect of malnutrition. The extent of malnutrition in such animals can be best evaluated by the decrease in the total circulating plasma proteins (column 9). The fall in the plasma chloride level can be seen to be quite marked, especially in the last two dogs in this series, in which vomiting during the last five to seven days of life was quite extensive.

These animals were permitted to have food and water which they ingested freely for six or seven days. Vomiting was rare during the first week of illness and during this time the plasma volume studies showed little change. During the second week, the loss of fluids and electrolytes was more marked, and apparently because of this and also because of a diminished intake there was a precipitous fall in the body water. The plasma volume changes can be seen to vary from -4 per cent to -45 per cent and the "available (thiocyanate) fluid" volume from 0 per cent to -27 per cent.

Because of the associated malnutrition in this colonic series, it was decided to study animals that did not have intestinal obstruction but from which food and water were withheld, thus evaluating the effects of starvation. The results on four such animals are shown in Table V. The plasma volume showed decreases of from 15 to 30 per cent in from three to seven days, and the "available (thiocyanate) fluid" decreased from 4 to 20 per cent.

The hematocrit and plasma protein concentration again did not reflect the plasma volume loss in a quantitative manner; in fact, the experimental

TABLE V
BLOOD STUDIES OF DOGS FROM WHICH FOOD AND WATER WERE WITHHELD

Dog No.	Days of Starvation	Hematocrit Cc./100 Cc.	Plasma Chloride	Plasma Protein	Plasma Volume	Percentage Change of Volume		Percentage Change in Total Circulating
			M. Eq./L.	Gm./100 Cc.	in Cr.	Plasma	Thiocyanate	Plasma Proteins
359	0	31.9	111.8	6.20	865			
	3	33.8	111.0	6.53	737	-15	-16	-10
	4	33.7	111.5	6.37				
358	0	36.7	110.2	6.02	647			
	2	39.6	110.8	6.25				
	4	40.1	111.8	6.07	528	-18	-4	-18
352	0	49.2	106.0	7.14	713			
	6	55.5	113.0	6.99	498	-30	-15	-32
	8	50.0	110.0	6.15				
338	0	42.1	114.6	5.81	850			
	5	51.4	121.4	6.36				
	7	52.9	121.2	6.41	600	-29	-20	-22

values were frequently about the same as the control levels. The loss in total circulating plasma proteins due solely to malnutrition was great (10 to 32 per cent). The plasma chloride levels were normal or slightly high, and yet because of the diminished extracellular fluid volume the total body electrolytes were lower following the period of starvation than in the control period.

COMMENT.—It seems pertinent, first of all, to enumerate the possible ways in which body water in intestinal obstruction might be diminished. Probably the most frequent cause for reduction is a diminished or inadequate fluid intake. As shown by the experimental work represented in Table V, animals which receive inadequate amounts of food and water may show decreases in body fluids which are great. This must also occur frequently in human patients to a varying degree. During the starvation, or reduced intake period, the elimination of body water continues, and, although the amount might be diminished, fluid is lost through the lungs, sweat glands and kidneys.

The second most frequently seen cause for a reduction of body water is abnormal losses. In cases of intestinal obstruction this occurs largely owing to vomiting. As Peters⁷ has repeatedly pointed out, the amount of vomiting is largely dependent on the intake of food and liquid. When fever is present, the loss due to sweating might be quite significant, and, occasionally, when the obstruction is partial, diarrhea may occur and contribute to the fluid loss. Naturally, gastro-intestinal secretions which accumulate above the point of obstruction or are removed by intestinal intubation might be considerable and frequently constitute as great a loss, if not greater, than fluid which is lost during emesis.

The diminution in body water by the two processes (decreased intake and increased output) thus may result in great decreases in plasma and interstitial water. The deficit of plasma proteins results largely from an insufficient caloric and nitrogen intake and an associated break-down of tissue proteins. Animals,⁸ and patients,^{9, 10} have been shown to be in a rather marked degree of negative nitrogen balance, especially during the early

periods of starvation, and when fever and infection are present. The change in the amount of total circulating plasma protein thus must depend largely on the degree of reduction in the nitrogen intake, the rate of destruction of plasma and other tissue proteins, and the reserve stores present at the onset of illness. The electrolyte loss may also be of considerable importance. If vomiting occurs or gastro-intestinal drainage is instituted, a significant decrease in the body electrolytes may result. As has been previously pointed out, such an electrolyte loss may lead to severe alkalosis if gastric secretions are lost, or to acidosis if duodenal fluid is lost, and thus cause a shift of fluid from the plasma and interstitial spaces where it is greatly needed into the intracellular compartments.¹³ When sodium is lost from the body, the plasma and the interstitial fluids are temporarily in an hypotonic state. To restore equilibrium two mechanisms operate: First, urine is excreted which has a low concentration of electrolytes; and, secondly, water passes from the extracellular phase into the intracellular compartment. Thus, when a primary electrolyte loss occurs, a diminution in the extracellular volume may occur due both to water loss in the urine and a water shift into the tissue cells.¹³

It should be stressed that the degree of body water loss can rarely be estimated from the plasma chloride concentration. In the various types of intestinal obstruction studied in this series at least one animal in each group (pyloric, jejunal, ileal and colonic) showed severe electrolyte loss as demonstrated by the plasma chloride concentration. However, as McIver and Gamble¹⁵ pointed out, in 1928, the loss of bile and intestinal fluid containing approximately the same amount of fixed base (sodium) and chloride as does plasma may occur. Such a loss will produce a reduction in the total amount of body electrolytes and a diminution in the plasma and interstitial fluid without altering the plasma chloride or bicarbonate concentrations. Thus, in some of the animals reported, a reduction of fluid and electrolytes occurred even though the plasma concentrations were high or normal. For example, Dogs 42-9 (Table II) and 42-13 (Table III) had extracellular fluid volume losses amounting to about one-third of their volume, and without any electrolyte loss one would expect a rise in the plasma chloride level to around 150 M. Eq. per liter. This does not occur normally because of the ability of the kidneys to excrete the excessive electrolytes and thus maintain the body fluid in an isotonic state and preserve a normal acid-base balance. However, when dehydration becomes severe, the body cannot supply adequate amounts of water for the formation of urine, or if kidney damage intervenes prior to this, a rise in the blood nitrogenous products, in the plasma chloride concentrations, and even occasionally in the total base (sodium or bicarbonate) occurs.

Besser,¹⁶ in 1940, reviewed the literature on intestinal obstruction, and summarized an earlier paper by Elman and Hartmann,¹⁷ in which they stated that low (ileocecal) obstruction in only rare instances caused death by changes in body fluids which resulted in circulatory and renal insufficiency

due to dehydration. Such work assumed that the extent of body fluids was unaltered because the concentrations of various blood constituents remained normal. As pointed out above, the blood chemistry may be normal even though dehydration is severe. The actual extent of electrolyte loss or gain can be estimated only by determining the total loss of circulating plasma chloride and interstitial fluid chloride levels and not by the changes in the plasma concentration.

The third cause for a reduction in the plasma volume is distention of the gastro-intestinal tract. As Gendel and Fine¹⁸ have shown, the loss of plasma might be great and might account for death *per se*. Gatch and Battersby¹⁹ have also pointed out that the loss might be large by this avenue and the damage to the vascular bed might be irreversible so that even with relief of the distention body water continues to be lost.

Aird,²⁰ using the vital red method for determining the plasma volume, states that the blood volume in some experimental animals with intestinal obstruction is depleted before death but says "this occurs only when intestinal distention is extreme." This view is not entirely in keeping with our data for several reasons: First, many of the animals reported in this paper, which showed moderate to large reductions in their plasma volume, were killed after the determinations were made, and autopsy showed little evidence of distention. Secondly, the results obtained in the animals which were not permitted to have food and water showed that the plasma volumes could be decreased significantly (30 per cent) without vomiting or distention being present. Therefore, it would appear that while distention is an important factor and may cause a rapid loss of plasma, the same may occur over a longer period in its absence.

Fine and Gendel²¹ also have stated "that when, and if dechlorination occurs in the course of intestinal obstruction it is by no means a crucial factor in the lethal effects of obstruction." In another publication²² they stated that "as the plasma volume falls the hematocrit rises. This increase in hematocrit is far greater than can be explained by dehydration, however severe." They also concluded that dehydration and electrolyte imbalance are not responsible for the greater part of the plasma loss.

This was undoubtedly true in their series, but it should be remembered that they studied intestinal distention *per se* over a period of hours rather than days, and that the effects of dehydration as seen in our animals could not be found in short-term experiments. Granted that distention alone can produce large alterations in the plasma volume and that it might often be the most important factor, it should also be borne in mind that just as great alterations in the plasma volume in intestinal obstruction can occur in its absence, due solely to dehydration and can also lead to just as serious results.

To lend further support to this view, Davis²³ has shown that by the injection of 25 per cent salt solution subcutaneously, all the pathologic findings of shock might be produced. Several such experiments were repeated

by us, and in each instance there was a marked progressive rise in the hematocrit and plasma protein concentration and, immediately after death, autopsy revealed the pathologic findings of shock. These animals showed various side-effects which are usually not seen in shock, such as twitchings of all extremities, even to the point of convulsions, and extremely high temperatures (rectal temperature in one animal, taken repeatedly for several hours prior to death, varied from 43° to $44.5^{\circ}\text{C}.$). On the other hand, dehydration produced by injecting 5 per cent glucose in distilled water (100 to 200 cc. per kilogram of weight) intraperitoneally, as described originally by Darrow and Yannet,^{24, 25} will produce a marked lowering in the plasma volume.¹³ If the animals are dehydrated sufficiently, all the pathologic changes of shock are present at death. These animals show the signs and symptoms characteristic of shock (cold extremities with a low temperature and hemoconcentration with a diminishing plasma volume).

The fourth factor which might lead to a diminution of the effective blood volume in intestinal obstruction occurs when strangulation of a loop of intestine takes place. Unpublished data,²⁶ from this laboratory, showed hemorrhage to occur into the intestine of several such animals, although occlusion of the blood supply to the obstructed loop was produced in each instance. Also serosanguineous peritoneal fluid was present. Factors which have been enumerated above (starvation, vomiting, and distention) undoubtedly also occur in patients when a loop of bowel becomes incarcerated or strangulated. In human patients an even greater difference might be encountered than is seen in the experimental animal, probably because of the wide variation in the degree and duration of strangulation or incarceration, and also because of differences in the degree of early vascular impairment. Gatch and Culbertson²⁷ have shown that the blood supply to a distended loop will be impaired if the distention is great enough. On the other hand, in patients the vascular supply might possibly be greatly reduced prior to the time distention occurs (volvulus or herniation of a loop). Thus, in strangulation, impairment to the blood supply of the affected loop undoubtedly occurs if the condition progresses far enough. It might take place early in some cases (mesenteric vessels occluded) or later in others (when distention takes place and the smaller vessels in the bowel wall are affected). When the mesenteric vessels are involved, hemorrhage may occur either into the obstructed loop or above or below it. Thus hemorrhage might occasionally be an additional factor in reducing the volume of circulating blood.

An attempt should be made to try to differentiate between a loss of plasma water and a loss of plasma protein. In starvation and vomiting there is initially just a loss of fluids and electrolytes. Malnutrition and an increased rate of catabolism (due to fever, infection, *etc.*) may reduce the body proteins and then, terminally, when the circulation is greatly impaired, there might also be an actual loss of protein through the capillary walls. Gatch and Battersby¹⁹ have shown that in gastro-intestinal dis-

tention, plasma water and proteins are lost, and certainly this also occurs in strangulation with or without hemorrhage. In a recent publication, Bowers²⁸ pointed out the degree of plasma protein loss which might occur in experimental appendicitis with peritonitis. While it has been known for some time that protein is lost with the formation of sterile or infected exudations, this possibility should also be kept in mind in intestinal obstruction. In several animals, which were not included in this series, because a second operation was performed to relieve the obstruction, purulent fluid, which contained a large amount of protein, was found in the peritoneal cavity at autopsy. Thus, in the presence of infection or gangrene in cases of intestinal obstruction, plasma water and proteins might decrease quite markedly. The severity of the symptoms or the rapidity of death from intestinal obstruction, therefore, depends on the number of factors which enter into the picture. In this paper the cause of death due to absorption of so-called toxic products has not been dealt with. While it is conceivable that such products might possibly exist, and even produce serious effects, it is believed that sufficient evidence has been presented to show that death can occur in intestinal obstruction at various levels purely from an excessive loss of body water and, hence, impairment to the vascular system (with or without renal dysfunction).

In the animals reported, wide variations in the hematocrit, protein concentration, and total circulating plasma protein levels occurred. Because of this, as has been previously stated elsewhere,^{10, 20 and 20a} it is believed that in most instances the hematocrit and plasma protein concentration, while they might show directional changes, cannot be employed to estimate quantitatively alterations in the plasma volume. It has been shown that the longer the period of malnutrition, the more inaccurate these levels become.

Many of the results in these animals were included in a previous publication²⁰ to lend support to the theory that contrary to the previous belief,^{30, 31} the plasma volume is not maintained initially at the expense of the interstitial fluid, and, thus, alterations in the hematocrit and protein concentration might be indicative of early as well as late changes.

In the treatment of intestinal obstruction all factors should be kept in mind. If this be done, and treatment is carried out accordingly, the mortality rate would then largely depend on whether or not irreversible changes had occurred (severe distention, gangrene or infection). In the event large amounts of plasma proteins are lost, it is easy to see why physiologic saline alone is of little value in restoring body fluids. It has been suggested that, because saline would not greatly prolong life in low intestinal obstruction, there was little electrolyte and fluid imbalance in such cases. This is obviously not true, unless exact replacements of saline, plasma, and whole blood were carried out daily and their rapid loss (due to infection, distention or hemorrhage) prevented. Then, in the event that death occurred and autopsy showed the typical pathologic findings, such a statement would be possible.

The gross and microscopic examination at autopsy showed the same pathologic findings in the animals which went to death as those described by Moon and Morgan²² (hemorrhagic changes in the lungs, submucosal intestinal hemorrhages, *etc.*). In no instance were such findings seen in the animals killed prior to death even though in some cases dehydration was severe. Such pathologic changes must, therefore, occur as a terminal event.

SUMMARY

The reduction of body water in intestinal obstruction might occur in one or more of the following ways:

1. Reduced intake.
2. Excessive loss (or normal loss and restricted intake).
 - a. Vomiting.
 - b. Perspiration.
 - c. Urinary.
 - d. Diarrhea.
3. Distention.
4. Strangulation.
 - a. With or without hemorrhage.
 - b. Transudation of fluid.
5. Infection.
 - a. Exudation of fluid.

Any one of the aforementioned items may cause death due to a peripheral vascular collapse, if allowed to progress for sufficient time, but more commonly in intestinal obstruction at least two or more are present.

A decrease in the body protein might result owing to:

1. Reduced intake of food.
2. Excessive destruction.
3. A loss of whole blood or plasma from the vascular system.

Because of such decreases, the hematocrit and protein concentration cannot be employed to estimate quantitatively the reduction in the plasma volume.

The wide variation in the signs, symptoms and course of clinical cases depends on the severity and number of the previously mentioned factors, and the degree and type of treatment. Success in treating patients would, therefore, depend on the recognition of the causes of loss of body water that exist and the restoration of these to normal (the correction of fluid and electrolyte balance and the replacement of the plasma protein loss). This cannot be accomplished if distention, vascular damage and infection cannot be corrected. Thus, it is evident that physiologic saline, plasma, or whole blood will continue to leak out of the vascular system unless the cause for the loss can be removed.

CONCLUSIONS

1. Evidence has been presented to show that dehydration resulting from intestinal obstruction (pyloric, jejunal, ileal or colonic) may be severe enough to cause death in itself if the condition exists for a sufficient time.

2. The amount of gastro-intestinal fluid lost varies greatly, depending on the level and degree of obstruction, and the amount and frequency of vomiting. The body water deficit, usually resulting from a diminished intake and an excessive loss, may be greatly accelerated when distention, strangulation, hemorrhage or infection occurs.

3. The rapidity of body water loss depends on the number of causes present and the severity of each. This explains the wide variation seen in the course of the disease in patients with intestinal obstruction.

4. The success of the treatment depends largely on the completeness with which the body water can be restored and on the prevention of further losses.

5. The hematocrit, plasma protein level, and the plasma chloride concentration cannot be employed to estimate quantitatively the decrease in the plasma volume.

6. The deficit in total circulating plasma proteins might be considerable in cases of intestinal obstruction, especially in those cases of long duration, and this loss is usually masked by hemoconcentration, and, thus, cannot be recognized by the plasma protein concentration.

REFERENCES

- ¹ Foster, W. C.: Acute Intestinal Obstruction. *J. A. M. A.*, **91**, 1523-1529, 1928.
- ² Gregersen, M. I., and Stewart, J. D.: Simultaneous Determinations of the Plasma Volume with T-1824 and "Available Fluid" Volume with Sodium Thiocyanate. *Am. J. Physiol.*, **125**, 142-152, 1939.
- ³ Gibson, J. G. II, and Evelyn, K.: Clinical Studies of the Blood Volume. IV. Adaptation of the Methods to the Photo-electric Microcolorimeter. *J. Clin. Invest.*, **17**, 153-158, 1938.
- ⁴ Barbour, H. G., and Hamilton, W. F.: The Falling-Drop Method for Determining Specific Gravity. *J. A. M. A.*, **88**, 91-94, 1927.
- ⁵ Van Slyke, D. D.: The Determination of Chloride in Blood and Tissues. *J. Biol. Chem.*, **58**, 523-529, 1923-24.
- ⁶ Wilson, D. W., and Ball, E. G.: A Study of the Estimation of Chloride in Blood and Serum. *J. Biol. Chem.*, **79**, 221-227, 1928.
- ⁷ Peters, J. P.: The Structure of the Blood in Relation to Surgical Problems. *ANNALS OF SURGERY*, **112**, 490-497, 1940.
- ⁸ Lusk, G.: The Science of Nutrition. 4th ed., Philadelphia, W. B. Saunders Co., pp. 75-117, 1928.
- ⁹ Brunschwig, A., Clark, D. E., and Corbin, N.: Postoperative Nitrogen Loss and Studies on Parenteral Nitrogen Nutrition by Means of Casein Digest. *ANNALS OF SURGERY*, **115**, 1091-1102, June, 1942.
- ¹⁰ Abbott, W. E., and Mellors, R. C.: Total Circulating Plasma Proteins in Surgical Patients with Dehydration and Malnutrition: Indications for Intravenous Alimentation with Amino-acids, *Arch. Surg.*, (in press).
- ¹¹ Gamble, J. L., and McIver, M. A.: The Acid-base Composition of Gastric Secretions. *J. Exper. Med.*, **48**, 837-847, 1928.
- ¹² Gamble, J. L., and McIver, M. A.: Acid-base Composition of Pancreatic Juice and Bile. *J. Exper. Med.*, **48**, 849-857, 1928.
- ¹³ Mellors, R. C., Muntwyler, E., and Mautz, F. R.: Electrolyte and Water Exchange between Skeletal Muscle and Plasma in the Dog following Acute and Prolonged Extracellular Electrolyte Loss. *J. Biol. Chem.*, **144**, 773-784, Aug., 1942.

- ¹⁴ Scudder, J., Zwemer, R. L., and Truszkowski, R.: Potassium in Acute Intestinal Obstruction. *Surgery*, **1**, 74-91, 1937.
- ¹⁵ McIver, M. A., and Gamble, J. L.: Body Fluid Changes due to Upper Intestinal Obstruction. *J. A. M. A.*, **91**, 1589-1592, 1928.
- ¹⁶ Besser, E. L.: Cause of Death in Cases of Mechanical Intestinal Obstruction. *Arch. Surg.*, **41**, 970-993, 1940.
- ¹⁷ Elman, R., and Hartmann, F.: Experimental Occlusion of the Terminal Ileum: Importance of Blood Chemical Changes in Causing Death. *Surg., Gynec. & Obst.*, **53**, 307-315, 1931.
- ¹⁸ Gendel, S., and Fine, J.: The Effect of Acute Intestinal Obstruction on the Blood and Plasma Volumes. *ANNALS OF SURGERY*, **110**, 25-36, 1939.
- ¹⁹ Gatch, W. D., and Battersby, J. S.: The Two Stages of Bowel Distention; A Study of Bowel Injury by Distention and its Effect on the Volume and Concentration of the Blood. *Arch. Surg.*, **44**, 108-118, January, 1942.
- ²⁰ Aird, I.: Morbid Influences in Intestinal Obstruction and Strangulation. *ANNALS OF SURGERY*, **114**, 385-414, 1941.
- ²¹ Fine, J., and Gendel, S.: Plasma Transfusion in Experimental Intestinal Obstruction. *ANNALS OF SURGERY*, **112**, 240-248, 1940.
- ²² Fine, J., Hurwitz, A., and Mark, J.: A Clinical Study of the Plasma Volume in Acute Intestinal Obstruction. *ANNALS OF SURGERY*, **112**, 546-556, 1940.
- ²³ Davis, H. A.: Pathology of Dehydration Shock. *Arch. Surg.*, **42**, 939-955, 1941.
- ²⁴ Darrow, D. C., and Yannet, H.: The Changes in the Distribution of Body Water Accompanying Increase and Decrease in Extracellular Electrolyte. *J. Clin. Invest.*, **14**, 266-275, 1935.
- ²⁵ Darrow, D. C., and Yannet, H.: Metabolic Studies of the Changes in Body Electrolyte and Distribution of Body Water Induced Experimentally by Deficits of Extracellular Electrolytes. *J. Clin. Invest.*, **15**, 419-427, 1936.
- ²⁶ Abbott, W. E., Peck, H., and Mellors, R. C.: Observations on the Circulatory System by Means of the Dissecting Microscope in Animals with Dehydration, Shock and Hemorrhage, (unpublished data).
- ²⁷ Gatch, W. D., and Culbertson, C. G.: Circulatory Disturbances Caused by Intestinal Obstruction. *ANNALS OF SURGERY*, **102**, 619-635, 1935.
- ²⁸ Bower, J. O., Terzian, L. A., and Pearce, A. E.: Changes in the Blood and the Composition of Peritoneal Exudate in Induced Spreading Peritonitis: A Preliminary Report. *Arch. Surg.*, **44**, 1091-1102, June, 1942.
- ²⁹ Mellors, R. C., Muntwyler, E., Mautz, F. R., and Abbott, W. E.: Changes of the Plasma Volume and "Available (Thiocyanate) Fluid" in Experimental Dehydration. *J. Biol. Chem.*, **144**, 785-793, Aug., 1942.
- ^{29a} Abbott, W. E., and Mellors, R. C.: Body Fluid Studies in Experimental Obstruction at Various Levels of the Gastro-intestinal Tract. *Surgery*, **12**, 445-449, September, 1942.
- ³⁰ Gamble, J. L., and McIver, M. A.: Body Fluid Changes Due to Continued Loss of the External Secretion of the Pancreas. *J. Exper. Med.*, **48**, 859-869, 1928.
- ³¹ Gamble, J. L.: Extracellular Fluid: Extracellular Fluid and its Vicissitudes. *Bull. Johns Hopkins Hosp.*, **61**, 151-173, 1937.
- ³² Moon, V. H., and Morgan, D. R.: Shock: The Mechanism of Death Following Intestinal Obstruction. *Arch. Surg.*, **32**, 776-788, 1936.

A STUDY OF PLASMA PROTEIN VARIATIONS IN SURGICAL PATIENTS

DANIEL CASTEN, M.D., MILTON BODENHEIMER, M.D.,
AND IRVING BARCHAM, M.D.
NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF DR. MILTON BODENHEIMER, HOSPITAL FOR JOINT DISEASES, NEW YORK, N. Y.

WHIPPLE¹ has recently stated: "It is our belief that the plasma proteins take an active part in the internal protein metabolism of the body, that they are built up rapidly, used in the body economy freely, and serve to supply practically all of the protein requirements of the cells of the body." The importance of hypoproteinemia in surgical patients has been stressed repeatedly.^{2, 3, 4} It is well known that many complications may develop in the postoperative period as a result of hypoproteinemia and that these may be prevented frequently by adequate prophylactic and therapeutic measures. We have previously pointed out that the fundamental causes of this deficiency state may not be known definitely although the liver has a rôle of great importance in maintaining an adequate level of the plasma proteins. However, there are many factors associated with, or related to, operative procedures which have a profound effect on the concentration of the plasma proteins. The presence of low plasma protein concentrations should be taken as an indication of a profound nutritional disturbance and the local manifestations, while important in themselves, assume greater importance as an indication of depletion of the reserve stores of protein and a general metabolic disturbance. These changes render the patient especially susceptible to infections and toxins. The present study is an attempt to determine: (1) The incidence of hypoproteinemia associated with operations, and the relationship to various procedures; (2) the factors which influence changes in plasma proteins; (3) the relationship between liver disorders and hypoproteinemia; and (4) methods of preventing and treating hypoproteinemia.

METHODS OF STUDY

A series of 215 surgical patients have been included in this study. These cases were selected from the surgical services of the Hospital for Joint Diseases as they were admitted, no attempt being made to segregate or select specific cases. Preoperative determinations of the total plasma proteins and hematocrit were made on every patient in addition to other blood chemical studies which were done when indicated. Blood specimens were taken postoperatively at 12- or 24-hour periods depending upon the nature of the case, and these specimens were examined for total plasma protein and hematocrit reading. The specimens, when practicable, were drawn early in the morning and no blood was taken while intravenous fluid was being

administered, except in emergencies. As a rule, parenteral fluids had been discontinued for at least two to four hours before the blood was withdrawn. Occasionally it was not possible to discontinue the administration of fluid. In these cases the rate of administration was slowed as far as possible and the blood drawn from the opposite arm. Fluid at all times was administered in volume and amounts calculated to maintain or restore normal fluid and electrolyte balance. The blood samples were drawn into Sanford-Magath hematocrit tubes containing 1 mg. of heparin. The technic of Scudder,³⁵ as outlined in his monograph on blood studies in shock, was followed in detail. The hematocrit tubes were centrifuged for one hour at 2500 revolutions per minute and the hematocrit read. The supernatant plasma was then used for determination of the total plasma protein, using the falling-drop method (Hamilton, Barbour apparatus). Three determinations were carried out on each sample and if a variation of over 0.2 Gm. was observed, the sample was discarded and the entire procedure repeated. This method was selected because of the rapidity of determination which it makes possible. While this does not give the protein fractions, it serves as an adequate guide in surgical cases, inasmuch as the albumin fraction is usually the variant and the globulin fraction varies little and is of slight significance from a surgical viewpoint.

The importance of plasma volume determinations particularly in the estimation of protein reserve is well recognized, but we have not carried out these studies because the procedures are time-consuming and not well adapted to clinical routine. We feel that frequent determinations of blood concentration and plasma proteins afford sufficient check for routine use. The significance of increasing hemoconcentration (as indicated by an elevated hematocrit reading) is well recognized as diagnostic of certain type of shock, dehydration, and decreased blood volume, but the equal importance of diminished blood concentration should not be overlooked. This may be associated with shock, as well as with hemorrhage and may also indicate decreasing circulating blood volume. Careful attention to the results of the hematocrit and plasma protein determination is sufficient, we feel, to act as a guide for therapy.

In addition, in a selected group of patients, determinations of liver function were made by the hippuric acid excretion test.⁵ This is performed as follows: The fasting patient is given 1.77 Gm. of sodium benzoate in 20 cc. of distilled water intravenously after having emptied the bladder. Two glasses of water (500 cc.) are given to the patient and the urine collected in exactly one hour, catheterization being employed if necessary. The content of hippuric acid in the urine is determined by the Quick method. Values of one gram or over are considered normal. We have used this test on several hundred patients and feel that it is probably the best single test for determination of liver function. This is particularly true in the non-jaundiced patient and in those with mild degrees of liver damage such as may be found associated with chronic gallbladder disease or thyrotoxicosis.

Many others have testified to the value of the hippuric acid test in determining the ability of the liver to withstand operative procedures.^{6, 7, 8} This function test measures the ability of the liver to synthesize amino-acetic acid. This is a very delicate function and one for which the liver has little or no reserve. It, therefore, enables us to detect very slight alterations in liver physiology.

Following the operative procedures, determinations of plasma proteins and hematocrit were made immediately and at intervals of 12 to 24 hours until the patient had completely recovered. The determinations were repeated for this period because it was noted that many cases developed a secondary or delayed drop after having once returned to normal.

TYPE OF OPERATIONS

There are many factors which influence the level of the plasma proteins and it is obvious that there will be different degrees of variation as a result of different operations. Among the immediate causes of plasma protein depletion are operative shock and blood loss. Other causes not so immediately apparent are: The previous nutritional state of the patient and the protein reserve; the degree, if any, of liver damage; and the effect of anesthesia, which may operate through its effect on the blood volume directly or on the liver.

Coller,⁹ and others, have shown that blood loss under ordinary circumstances varies according to type of operation. The amount of blood lost during a hernioplasty or appendectomy may be no more than 100 cc., while during a radical breast amputation it may total 1000 cc. Similarly, degrees of operative shock may vary. Handling of intestines may cause a marked degree of plasma loss from the vascular channels, and operations on bones or extremities may cause a similar loss. These two factors, blood loss and shock, will cause an immediate loss of plasma proteins and a decrease in the protein level of the plasma. Since most patients have a large reserve of proteins for plasma protein regeneration the deficit will soon be corrected if, indeed, in the interval it has not been restored by whole blood or plasma transfusions. In patients who come to operation in a poor nutritional state as a result of vomiting, diarrhea, dietary restrictions, or other causes, the reserve proteins may have been depleted. In addition, this malnutrition may have affected the liver so that the synthesis of stored protein into plasma protein is impaired, and the result will be prolonged low levels of plasma proteins.

In order to evaluate properly the results obtained in this study, the figures were subjected to a careful statistical analysis. It is well known that the larger the group of patients under consideration, the more significant will be the results. The significance of a given set of figures is usually determined by the calculation of the standard error and the relative deviate. This standard error is commonly designated by σ (sigma), and is a measure of the amount that a given percentage could vary due to experimental error

or chance alone. In Table I, this column of figures is based on the percentage of cases showing a fall in proteins for the whole group and the size of each particular group.

The relative deviate is the ratio of x to σ , where x is the difference between the percentage observed for a particular group and the overall percentage for all groups, and σ is the standard error. It is common statistical practice to take a relative deviate of 2.5 as the limit of significance because this represents the point beyond which an observed percentage could be expected to be only one per cent of the time, or once in a hundred similar experiments, due to chance alone. When an observation is such that it could be expected to be due to chance only once in 100 experiments the inference is that it is not the result of chance variation but that it is the result of a set of characteristics or conditions which make the group under consideration different from the other groups or from the average of the other groups combined. This is what is meant by a significant difference.

TABLE I
INCIDENCE OF POSTOPERATIVE DECLINES IN PLASMA PROTEINS IN VARIOUS TYPES OF OPERATION

Type of Operation	No. of Cases	No. of Cases	Per Cent	Cases with Fall in Proteins	
				Standard Error (σ)	Relative Deviate (x/σ)
1. Appendicectomy for acute appendicitis.....	23	16	69.6	9.65	0.07
2. Cholecystectomy for cholecystitis or cholelithiasis	27	22	81.5	8.91	1.41
3. Major procedure on the gastro-intestinal tract..	26	26	100.0	9.07	3.43
4. Operations for acute abdominal emergencies....	19	15	79.0	10.62	0.95
5. Hernioplasty for inguinal hernia.....	18	4	22.2	10.91	4.28
6. Orthopedic operations.....	34	24	70.6	7.93	0.21
7. Thyroidectomy for Graves' disease.....	17	12	70.6	11.23	0.15
8. Gynecologic operations.....	29	18	62.1	8.59	0.79
9. Miscellaneous operations.....	22	11	50.0	9.87	1.91
Totals.....	215	148	68.9	3.16	

On the basis of the foregoing, the results of a series of 215 cases were analyzed (Table I). Of these 148 patients (68.9 per cent) showed a significant fall (more than 0.5 Gm.) in their plasma proteins following operation. A standard error of 3.16 per cent indicates that the observed percentage could be expected to vary so that in repeated experiments with groups of 215 patients in only 95 experiments out of 100 it might be expected to be between 62.6 and 75.2 per cent. This statement is based on the following assumptions:

(1) That the cases represent a random sample of the conditions under discussion. No attempt was made to select particular patients and the cases were studied essentially in the order in which they were admitted to the surgical wards.

(2) That a fall in plasma proteins is an objective observation which is not subject to varying interpretation by different observers. No fall in protein was included unless it exceeded 0.5 Gm. Each blood sample was subjected to three plasma protein determinations and if the difference was greater than 0.2 Gm. the sample was discarded and another blood specimen drawn.

(3) That the figure of 68.9 per cent represents the average of the various percentages which would be obtained in repeated experiments. While this is not necessarily true it is accepted because it is impossible to make a better assumption.

In many of the patients the declines occurred despite blood or plasma transfusions at the time of operation. Occasionally the fall in proteins was to a subnormal level but more frequently the plasma protein level was considered normal, although from 1 to 2 Gm. below the preoperative level. A concomitant decrease in the hematocrit reading was frequently observed, particularly in those patients in whom the amount of blood lost at operation was excessive. Insofar as possible, this was corrected by appropriate fluid therapy.

Of the nine different types of operations performed upon these 215 cases, only the group of major gastro-intestinal operations showed a significantly higher incidence of protein loss than the group as a whole. The series of 26 cases is certainly large enough to indicate that a fall in protein will occur in operations of this type more frequently than in other operations, although from a statistical point of view it is not possible to state that this fall must occur in every major gastro-intestinal procedure.

The importance of these findings is obvious. Patients in this category have frequently suffered depletion of their reserve stores of protein prior to operation. Add to this a high incidence of significant protein loss as a result of operation, and a true hypoproteinemia frequently ensues. The clinical complications resulting from this state invariably contribute to a prolonged morbidity and an increased mortality.

At the other extreme, hernioplasty showed an incidence of protein fall significantly different from the total group (relative deviate 4.28). In these cases we can expect a decidedly lower frequency of diminished protein levels.

Cholecystectomy and operations for acute abdominal emergencies showed a higher percentage than the average (81.5 and 79.0 per cent, respectively). However, the relative deviates in these groups are below 2.5 and, therefore, it is not possible, statistically, to say that figures approaching these percentages would be found in all similar groups of cases. Obviously a larger series must be studied. Further information can be obtained by correlating these figures with those of liver function (Table II). This will be discussed subsequently.

It is in these groups, in which the relative deviate approaches but does not reach a level that can be considered truly significant, that clinical judgment must be exercised carefully. In acute abdominal emergencies, the added factor of shock is so frequent that this group deserves the most careful preoperative and postoperative care. In patients undergoing cholecystectomy the status of the liver, not uncommonly damaged as a result of prolonged gallbladder disease, must be accurately ascertained.

In all groups when the relative deviate is less than 2.5 the indication is

merely that for the size of the group the difference in percentage is not sufficiently large to be called significant. For example, considering the group of cholecystectomies, if the same percentage were to be found in a group of 85 similar cases rather than in 27 cases, the difference would be significant. Further studies are being conducted along these lines at the present time.

One must realize that statistical evaluation is valueless without clinical judgment and a thorough appraisal of the patient. Many factors resulting from the nature of the disease and the operative procedure, as well as from the nutritional status of the patient, must be considered in attempting to prognosticate the changes in the plasma proteins. For example; a patient undergoing cholecystectomy or thyroidectomy in whom the various liver

TABLE 11
SUMMARY OF CASES INCLUDED IN THIS STUDY

Type of Operation	No. of Cases	Total No. of Cases	No. of Cases with Fall in Proteins	No. of Cases without Fall in Proteins
1. Appendectomy for acute appendicitis:		23	16	7
Nonperforated	17			
Perforated.....	6			
2. Cholecystectomy for cholecystitis or cholelithiasis		27	22	5
3. Major procedure on the gastro-intestinal tract:		26	26	0
Gastro-enterostomy.....	8			
Gastrectomy.....	6			
Intestinal anastomosis and enterostomy.....	4			
Intestinal resection for carcinoma... ..	4			
Choledochostomy.....	3			
Cholecystogastrostomy.....	1			
4. Operations for acute abdominal emergencies:		19	15	4
Ruptured peptic ulcer.....	4			
Intestinal obstruction (gallstone).....	1			
Acute pancreatitis.....	3			
Ruptured abdominal viscus.....	1			
Strangulated hernia.....	2			
Evisceration.....	1			
Pelvic abscess.....	1			
Subphrenic abscess.....	2			
Celiotomy for peritonitis.....	4			
5. Hernioplasty for inguinal hernia.....		18	4	14
6. Arthopedic operations:		34	24	10
Arthrodesis.....	8			
Tendon operation.....	6			
Arthrotomy.....	3			
Spine fusion.....	10			
Open reduction of fracture.....	1			
Osteotomy and bone resection.....	6			
7. Thyroidectomy for Graves' disease.....		17	12	5
8. Gynecologic operations:		29	18	11
Vaginal plastics.....	12			
Hysterectomy.....	11			
Salpingo-oophorectomy for carcinoma and abscess.....	6			
9. Miscellaneous operations:		22	11	11
Closure of colostomy stoma.....	2			
Prostatectomy (1st & 2nd stage).....	5			
Resection of hypogastric plexus.....	1			
Tumor of abdominal wall.....	1			
Hemithyroidectomy for nontoxic goiter.....	7			
Excision of thyroglossal cyst.....	2			
Excision of parathyroid adenoma.....	1			
Radical mastectomy.....	3			
Totals.....		215	148	67

function tests reveal deficient liver activity must be expected to develop a sustained plasma protein deficit more often than one whose liver function is adequate.

When a patient is debilitated as a result of the disease process, partial or complete intestinal or pyloric obstruction, prolonged dietary restrictions, draining biliary or intestinal fistulae, diarrhea or prolonged suppuration, this factor must be carefully evaluated.

In other words, one must apply the statistical information obtained from these studies with due consideration of each patient as an individual problem.

In Table II the various cases which made up the total are listed. This is included merely to indicate the type of case which more frequently suffered from loss of proteins, but no one group is large enough for statistical analysis.

These studies are being extended now by the authors in a series of operations on laboratory animals. In dogs, for example, many factors are controllable which in the patient are subject to unpredictable variations. An attempt is being made to control the nutritional status, measure adequately the blood loss, control the nitrogen balance, and maintain blood concentration at a fairly constant level. We feel that these studies will supply further information unobtainable from the study of surgical patients.

In general, it can be said that the occurrence and extent of plasma protein depletion following operations depend upon the interrelationship of various factors. Poor nutrition, poor liver function, severe anemia, shock, hemorrhage, and prolonged operations, unfavorably influence the plasma proteins. Patients in good condition, undergoing operations such as hernioplasty which are complicated by none of these factors, rarely exhibit any change in their proteins.

The duration of the diminished concentration of proteins depends on many factors. Some of these will be discussed subsequently (liver factor and amount of protein reserve). As a rule, the diminution was transitory and return to normal occurred within three or four days. Other cases showed prolonged low levels and intensive therapy was essential to restore the normal concentration. When the loss of plasma protein was due to blood loss or shock, the deficit was quickly restored, but when other factors came into play, the time was prolonged proportionate to the extent of the operating factors (see case reports).

THE RÔLE OF BLOOD LOSS AND SHOCK

Every operative procedure is associated with some degree of blood loss. Usually this is insignificant, and even when fairly large amounts are lost, the deficit is quickly overcome. It seems apparent that a single hemorrhage of less than 500 cc. can be quickly compensated for and cause little or no change in the concentration of plasma proteins. Operative shock, on the other hand, resulting as it does, in diminished circulating blood volume and usually in hemoconcentration does cause alterations in the plasma proteins. A combination of both factors is responsible in most cases for a drop in the

plasma protein concentration of from 0.5 to 1.0 Gm. in the immediate postoperative period. This loss is quickly restored by the body in normal circumstances unless shock is severe or hemorrhage marked. When, however, the protein reserve has been depleted or the liver is damaged, restoration is delayed or absent and intensive therapy must be instituted.

RELATION OF ANESTHESIA TO CHANGES IN PLASMA PROTEIN

It is difficult to analyze the effect of one factor out of many on the plasma protein levels. Long operations requiring large amounts of anesthetic agents are also associated very frequently with excessive blood loss and some degree of shock, and these factors cannot be adequately segregated. However, it was observed that a definite relationship exists between the duration of anesthesia and changes in the proteins (Chart I). This correlation is very definite, as shown in Chart I, but it might be better to compare the duration

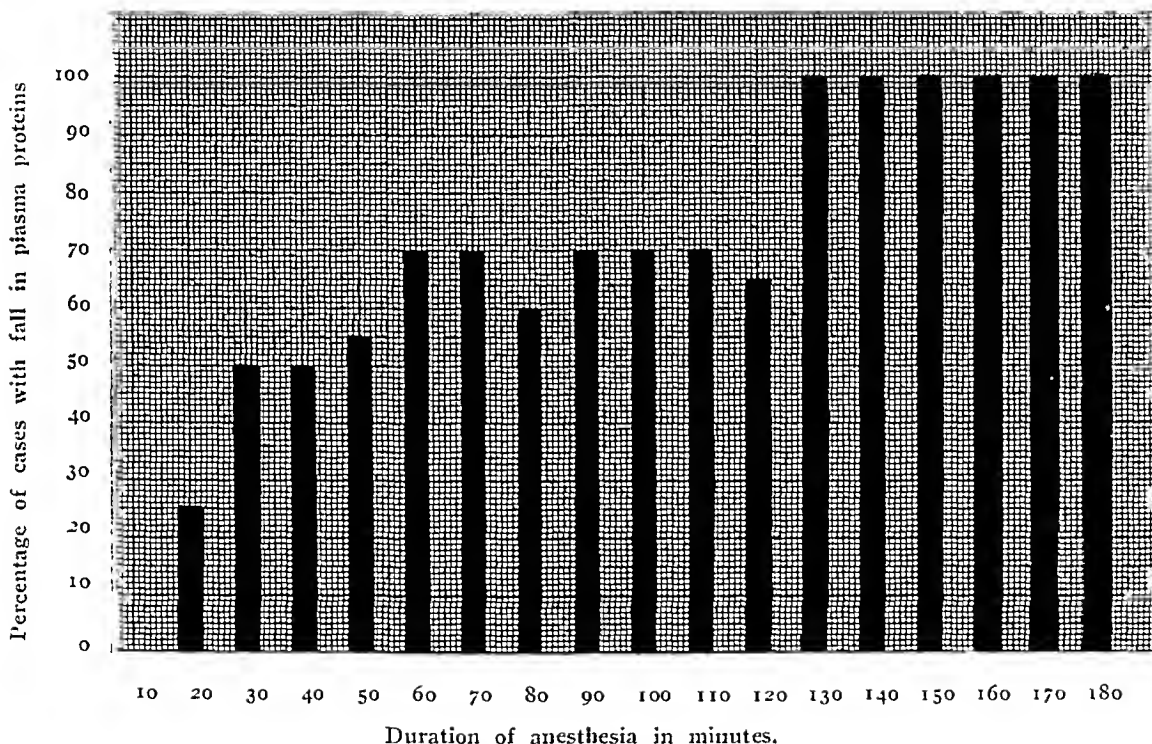


CHART I.—Relationship between duration of anesthesia and incidence of plasma protein decline.

of operation rather than duration of anesthesia, to the incidence of protein decrease. In operations under one hour, from 50 to 60 per cent of patients showed a decrease in plasma proteins, while in operations lasting over two hours, all cases showed significant falls. These figures are interesting, but an analysis of the various anesthetic agents employed in these cases, in an attempt to correlate the effect of various types of anesthesia with falls in plasma proteins, showed no significant variations.

The effect of anesthetic agents on the liver and on blood volume has been repeatedly studied. Ether, chloroform and cyclopropane are definitely toxic to the liver in certain concentrations. Likewise, they cause diminution in blood volume, principally in the plasma constituent. Procaine, used for

cent in the group with poor liver function and 50 per cent in the group with normal liver function) yields a relative deviate of 5.2 which is well beyond the limit of significance. In other words, patients with diminished liver function can be expected to show a postoperative fall in plasma protein much more frequently than those with normal function. This trend is extremely suggestive and the conclusion almost inescapable. Unquestionably, two factors have operated in these cases: (1) A depletion of protein stores because of prolonged poor liver function; and (2) an inability of the liver to synthesize rapidly enough plasma protein to replenish that lost as a result of the operative procedures (blood loss, shock, anesthesia, *etc.*). In addition one might postulate the existence of a vicious cycle, inasmuch as continued low plasma protein concentrations and depleted protein reserves may have a harmful effect on liver structure and function. It was our impression, also, that the response in protein concentration as a result of blood or plasma transfusion in these cases was not as sustained, although usually as prompt, as in other cases whose liver function showed no evidence of deterioration.

It is of great significance to the surgeon therefore, that control of plasma protein formation and protein storage is a function of the liver and that in many patients and especially in certain groups of patients, the function of the liver is impaired. In these cases, the incidence of hypoproteinemia and of decline in the protein levels to low normal values will be extremely high and the postoperative course will be correspondingly stormy. The indications for therapy are derived from these facts.

PROPHYLAXIS AND TREATMENT

It is evident from the preceding data that certain types of surgical patients will probably lose considerable amounts of plasma proteins as a result of operative procedures, while in other groups the loss will be insignificant and rapidly restored. With the latter, we are not particularly concerned, but in the former group certain problems of therapy are of great consequence. From a therapeutic standpoint this group can also be divided into two subgroups:

Subgroup I.—In this classification fall those patients who are about to undergo certain major surgical procedures which we know are frequently or usually associated with a definite decline in the plasma protein levels. The liver function is normal, but the preoperative level of the plasma protein may be either normal or slightly lowered. It is very important in these cases to attempt to assess the presence and amount if any, of deterioration in the reserve stores of protein. Some patients may have normal values which are being maintained at the expense of exhaustion of the protein stores. While this may be difficult to evaluate by laboratory methods the clinical history is of great importance. The length of the illness, the previous dietary regimen, the probability of absorption of nutritive elements from the ingested foods and the presence of subclinical or clinical avitaminosis are guides to a proper evaluation. Of course, if the protein levels are low, one must assume that

the reserve has been more or less exhausted. If one so decides operation must be deferred except in the gravest emergency until the depleted proteins are replenished. This may be done by several methods. The best and most practical route of administration is by mouth. This is the natural route for the absorption of the products of protein metabolism and is usually the most efficacious. A high protein diet for one to two weeks usually gives excellent results. If for any reason this cannot be administered, concentrated amino-acid preparations may be used. We have used these on many patients in this group with satisfactory results and they have the further advantage of being easily administered through a duodenal tube if necessary. In order to obtain the maximum benefit from the protein diet or from the amino-acids, it is important to remember that all protein foods do not effect equal increments in plasma protein production. Certain key amino-acids are essential for this synthesis, and among these are cystine, tryptophan, tyrosine, leucine and glutamic acid. A definite quantitative difference in plasma protein synthesis can be obtained by feeding various amino-acids.¹⁸ Milk, wheat, and eggs have a high cystine content and are, therefore, valuable in the diet. If amino-acids are fed as such, cystine and tryptophan should be present in large amounts. Preparations derived from casein, with tryptophan added, usually meet these requirements. If, for any reason oral feeding is interdicted, the intravenous route must be employed. For this purpose nothing gives results comparable to plasma transfusions. These should be given repeatedly and in large amounts and should be given to meet the requirements of the patient and not the convenience of the individual blood donor. Fortunately, with the increasing prevalence of blood banks the former usual arbitrary amount of 500 cc. per transfusion is rapidly becoming obsolete and transfusions of 1000 to 1500 cc. of blood or plasma are frequently administered with excellent results and no untoward reactions. In our experience the use of intravenous amino-acids has not been very successful, but we have not used this method extensively. Once the protein reserve and blood levels have been restored, operation may be safely undertaken.

In those patients whose protein stores are not depleted our concern is to prevent excessive declines in the plasma protein concentration. This drop in plasma proteins associated with operation will probably be transient and easily overcome by suitable administration of whole blood or plasma. The best guide to the quantity of blood and plasma required are serial studies of the hematocrit values and plasma protein concentration. It has been our experience that a transfusion of 500 cc. to 1000 cc. of plasma immediately preceding or during operation will carry these cases through any but the most shocking procedures.

Subgroup II.—This includes those patients in whom an impairment of liver function can be demonstrated and who are about to undergo major surgical procedures. In this group, also, the protein levels may be normal or low but in all probability, there has been some depletion of the protein stores. We are faced, in these patients, not only with the problem of restor-

ing the reserve stores of protein but with improving liver function, and in addition protecting the liver from further impairment of function as a result of anesthesia, operative shock and anoxemia.

Glucose has long been considered the substance *par excellence* for improving liver function. It is not to be denied that glucose in sufficient quantities does exert a markedly beneficial effect. It is the principal source of energy for the body mechanism and has the specific physiologic effect of sparing proteins. Recent evidence,^{19, 20, 21} however, has indicated that proteins are probably much more efficacious in restoring and maintaining good liver function. This experimental evidence points out that livers with a high lipid content are much more susceptible to toxins than those with a low lipid content. Wells³¹ has suggested that a large amount of liver fat results in a retention of lipid soluble hepatotoxic agents. It has been known for many years that fatty changes in the liver are associated with poor function. Proteins are effective in reducing liver fat.

The therapeutic effect of proteins is probably two-fold in patients with liver damage. In the first place, regeneration of body tissues requires ample protein supplies, and, secondly, protein undoubtedly has a specific effect in protecting the liver from injury. This action is probably a result of the lipotropic activities of certain amino-acids. Moise and Smith,²² Miller, Ross and Whipple,¹⁹ Goldschmidt, Vars and Ravdin,²⁰ Messinger and Hawkins,²³ and Perlman, Stillman and Chaikoff²⁴ have demonstrated the protective effect of proteins on the liver. Certain substances are known to be lipotropic; that is, they mobilize liver lipid and make it available for easy disposition. Lipocaic, choline and lecithin have marked lipotropic activity. Of the amino-acids, methionine and cysteine are the principal lipotropic agents. The former is more efficacious, inasmuch as cysteine has only a temporary lipotropic effect. In fact, after prolonged administration, it may exert an opposite effect. Other amino-acids including glycine, alanine, tyrosine, taurine, glutamic acid, and proline have no lipotropic activity. Choline is thought to be necessary for the action of any lipotropic substance. This may account for the deterioration of liver function in patients with biliary fistulae and persistent loss of bile. It is significant that cysteine is a key amino-acid for plasma protein regeneration also, while methionine is of no value in this process, but is more important for its lipotropic activity.

The foregoing evidence has a definite clinical application. It can be said that the most favorable diet for patients in this group should contain ample carbohydrate for energy purposes and to spare protein, ample protein containing sufficient amounts of lipotropic substances, and as little fat as is compatible with a palatable diet. Meat, in general, is not satisfactory, inasmuch, as even lean meat contains considerable fat. Channon and Wilkinson²⁵ state that a diet in which more than 14 per cent of the total calories are obtained from proteins will exert a marked lipotropic action. Casein, or foods high in casein are undoubtedly the best. Tucker and Eckstein²⁶ demonstrated the greatest decrease in liver fat with a 20 per cent casein diet.

A hospital diet containing 75 per cent of carbohydrates, 20 per cent of proteins (no meat) and 5 per cent fat will fulfill these requirements.

If food cannot be taken by mouth the same considerations should govern the parenteral therapy. However, it is difficult to supply sufficient glucose intravenously to meet the energy requirements of the body. A total of 1200 calories daily is the net result of 3000 cc. of 10 per cent glucose solution. The disadvantages of parenteral glucose are two-fold: first, the inconvenience of daily intravenous therapy and the danger of thrombosed veins, and secondly, the inadequacy of the amounts administered and the probability that glucose by mouth is more efficacious in its action on the liver than intravenous glucose. It is preferable whenever possible to supplement the intravenous therapy with some carbohydrate by mouth. This may be given as concentrated glucose solution.

Protein is best given parenterally in the form of plasma. While amino-acids have been used with some success by others, we have been unable to show any beneficial effect on the liver or any sustained rise in the plasma proteins by this method. However, our experience has not been very large with intravenous amino-acids therapy. One point is worth noting in this connection. It has been stated previously that cysteine exerts an initial lipotropic effect but prolonged administration nullifies this early action. It is thought that the cysteine which is present in plasma does not show this late change however, and plasma may be given indefinitely for its lipotropic action. This may account for our failure to realize any appreciable benefit with amino-acid solutions while with plasma the results were most encouraging.

Other measures have been suggested to improve liver function. The administration of Vitamin B₁ may be of value. Connor²⁷ has shown that deficiency of this vitamin may cause fatty infiltration of the liver. Furthermore, Vitamin B-complex is necessary for certain intermediary stages of carbohydrate metabolism and oxidative reactions in the tissue cells. The importance of this adjuvant when large amounts of carbohydrates are being fed to the patient is obvious. Bile salts and liver extracts are also indicated in certain cases. The marked lipotropic activity of choline has been mentioned and liver extract is rich in choline. The bile salts of taurocholic and glycocholic acids may have a similar effect. It is certainly well known that excessive loss of these bile salts has a deleterious effect on liver function.^{28, 29, 30} Bile salts administered orally also increase the arterial blood flow to the liver,²⁸ a real consideration in combating anoxia. Schmidt, Walsh and Chesky³¹ have found that insulin causes improvement in poor liver function associated with toxic thyroid disease. They feel that the damaged liver due to thyroid disease reacts differently to insulin than the normal liver in which it is well recognized that insulin is of little value in promoting glycolysis.^{32, 33} Further observations are undoubtedly necessary to determine the effect of insulin on livers damaged as a result of other conditions. We have not used it on the patients in this survey.

It was our experience with patients in this group that marked improvement occurred within two weeks as a result of the therapy instituted, except in some patients whose hippuric acid excretion was below 0.3 Gm. While it was not always possible to restore hepatic function to normal, we usually obtained satisfactory improvement, as manifested by a definite increase in the hippuric acid excretion. The optimum time for operation was occasionally difficult to determine and depended on many individual variations. The concomitant improvement in the protein reserve and the return to normal of the plasma protein values as a result of treatment directed at improving liver function are factors which aid in making a decision. In this group of patients we also observed a postoperative decrease in liver function below the maximum preoperative level, in spite of our prophylactic measures. The diminution was usually transient, but served as a danger signal and indicated the importance of fortifying the liver before operation.

In this second group, as contrasted to the first, in whom hepatic function was normal, extreme vigilance was required for many days after operations to forestall delayed protein declines. In the first group, once the immediate postoperative fall in proteins was compensated for, the level remained stationary unless complications developed. In the second group, however, even though improvement in liver function had been obtained, the return to normal of the plasma proteins was delayed, and was subject to many fluctuations. Continuation of the preoperative regimen was found to be essential to rapid and uncomplicated recovery.

The following case reports were selected in an attempt to illustrate more graphically the problems involved in the prophylaxis and treatment of the various phases of protein depletion and concomitant liver dysfunction.

CASE REPORTS

Case 1.—A. A., Hosp. No. 90176. Acute suppurative appendicitis. Appendectomy. A drop in plasma protein concentration of 1.1 Gm.% occurred within 48 hours, despite a simple operative procedure. Return to the preoperative level did not take place until the eighth day. No special therapy was employed. We believe that there is a continuing loss of plasma into the peritoneal cavity for several days after operations for acute appendicitis, and this frequently accounts for prolonged diminution in the protein levels.

Case 2.—F. A., Hosp. No. 88980. Appendiceal abscess. Appendectomy and drainage (wound packed open with iodoform gauze). Preoperative levels: Plasma proteins 7.0 Gm.%; hematocrit 42%. The protein level was maintained fairly well for two weeks. During this period drainage from the wound was profuse, and the patient had a moderate febrile reaction. The food intake was limited. The protein concentration began to fall quickly at the 14th day, probably due to exhaustion of protein reserves. This decline persisted until the 36th day (plasma proteins 6.2 Gm.%; hematocrit 42%), at which time intensive amino-acid therapy by mouth was instituted. Recovery was rapid after this point. Incidentally, during the first five weeks, wound healing was very slow but immediately after beginning amino-acid therapy a marked increase in the rate of granulation of the wound was observed.

Case 3.—R. K., Hosp. No. 89481. Chronic cholecystitis and cholelithiasis. Cholecystectomy. Preoperative studies indicated good liver function, normal plasma protein concentration, and apparently adequate protein reserves (plasma proteins 7.2 Gm.%;

hematocrit 44%; hippuric acid excretion 1.24 Gm.). Operation was carried out without any special preparation and the postoperative course was uneventful. There was an immediate and definite drop in both protein levels and liver function (plasma proteins 6.3 Gm.%; hematocrit 42%; hippuric acid excretion 0.49 Gm.), probably as a result of blood loss, operative trauma and anesthesia, but the declines were transient and a return to normal figures was noted on the 9th postoperative day. For purposes of therapy this patient should be classified in Subgroup I.

Case 4.—M. R., Hosp. No. 90200. Chronic cholecystitis and cholelithiasis. Cholecystectomy. Liver function studies indicated very poor function, and the low hematocrit and plasma protein figures indicated depletion of protein stores and a moderate secondary anemia (plasma proteins 6.1 Gm.%; hippuric acid 0.10 Gm.; hematocrit 33%). Dietary therapy was instituted for two weeks preceding operation, and while improvement in the protein concentration was satisfactory, liver function remained poor (0.51 Gm.). At operation, a walled-off pericholecystic abscess was found. The postoperative course was stormy, with elevated temperature and increased pulse rate for almost one week. With continuation of the dietary regimen, liver function gradually improved and the protein figures reached the preoperative level on the 14th postoperative day. This case was definitely in Subgroup II. More intensive protein therapy should have been administered in the form of plasma or whole blood transfusions.

Case 5.—A. C., Hosp. No. 89875. Graves' disease. Thyroidectomy. Liver function was markedly depressed but the proteins were normal (plasma proteins 6.6 Gm.%; hematocrit 46%; hippuric acid excretion 0.39 Gm.). Fairly intensive preoperative therapy was administered, but emphasis was placed on the thyroid rather than on the liver. A moderate postoperative crisis developed, associated with substantial protein depletion. Glucose and proteins were fed in large amounts with a satisfactory but very slow response.

Case 6.—C. P., Hosp. No. 86521. Graves' disease. Second-stage hemithyroidectomy. In the interval between operations the liver function and protein reserves were thought to be restored to normal (plasma proteins 6.7 Gm.%; hematocrit 33%; hippuric acid excretion 1.2 Gm.). However, the operative time was prolonged to two hours, and there was moderate bleeding. The effect on the protein was marked and sustained, a drop to 5.4 Gm.% occurring within three days after operation. On the 8th day the values had returned to normal. Apparently, this patient had not been sufficiently fortified for operation.

Case 7.—S. M., Hosp. No. 87843. Toxic adenoma of the thyroid. Hemithyroidectomy. Because of the satisfactory results of liver function tests and the adequate plasma protein level (plasma proteins 7.2 Gm.%; hematocrit 46%; hippuric acid excretion 1.5 Gm.%) no special treatment was thought necessary beyond that directed at the toxic thyroid disease. As in the preceding patient, the postoperative decline in protein levels and hippuric acid excretion was significant and fairly prolonged. The plasma proteins declined to 6.0 Gm.% on the third day, and remained low for over one week.

Case 8.—B. R., Hosp. No. 87569. Nontoxic adenoma of the thyroid. Hemithyroidectomy. The preoperative nutritional status was good (plasma proteins 7.9 Gm.%; hematocrit 45%; hippuric acid excretion 1.14 Gm.) and operation was performed the day following admission to the hospital. An immediate decline of 1.3 Gm.% in the protein values was observed, probably the result of excessive blood loss during a two hour operation. The return to normal was rapid, however, indicating that protein reserves were ample. This patient would be classified in Subgroup I, as contrasted to the preceding cases of toxic thyroid disease.

Comment.—A study of the four preceding cases of thyroid disease indicates the necessity for appreciating the significance of the liver and the protein reserves. Patients with toxic thyroid disease may show normal liver function preoperatively but they are potential "liver weaklings" and the effects of operation, blood loss, anesthesia and the resultant often prolonged

anoxia may be disastrous. Prolonged preparation not only for the hyperthyroidism, but for the liver is essential. We believe that more frequent blood or plasma transfusions would decrease the incidence of postoperative thyroid crisis.

Whereas the decline in proteins in the nontoxic cases is of very short duration, in the patients with hyperthyroidism the return to normal is delayed and is associated with postoperative impairment in liver function. The usual high carbohydrate diet which is fed to these cases preoperatively is insufficient and should be replaced by a diet rich in protein and very low in fat.

Case 9.—C. G., Hosp. No. 89429. Chronic, perforating duodenal ulcer. Subtotal gastrectomy. Preoperative studies of liver function and plasma proteins revealed normal levels (plasma proteins 7.0 Gm.%; hematocrit 42%; hippuric acid excretion 0.85 Gm.). At operation, a transfusion of 500 cc. of whole blood was given. Despite this, a marked decline in proteins to 5.3 Gm.% occurred immediately, and persisted for 16 days. On the tenth day, amino-acids were given orally, and continued daily. The effect was not manifested for several days however, but eventually a definite gain was observed. The amino-acids therapy was started at the time when the protein concentration was definitely below the edema level, and peripheral edema was present. While the patient had normal liver function and should be classified in Subgroup I, we feel that in common with most patients with chronic peptic ulcers she had a marked depletion of her protein reserves.

Case 10.—L. C., Hosp. No. 90438. Posterior wall gastric ulcer, with perforation into the pancreas. High subtotal gastrectomy. A week of preparation with a high protein diet before operation was thought to be adequate, although hepatic function was still subnormal (plasma proteins 6.5 Gm.%; hematocrit 37%; hippuric acid excretion 0.64 Gm.). During the operation 500 cc. of plasma were administered. An immediate rise in proteins took place followed by a moderate decline of 1 Gm.%. The hippuric acid excretion also diminished. A slow upward swing occurred during the next 10 days, but upon discharge from the hospital, on the 13th postoperative day, the preoperative levels had not been reached. In this patient, again, a fairly normal plasma protein concentration was maintained at the expense of exhaustion of the protein reserves and the customary restoration of proteins lost as a result of operation was delayed and inadequate.

Case 11.—L. B., Hosp. No. 88177. Carcinoma of the stomach at the esophago-gastric junction. Gastrectomy. The preoperative protein level was normal, and the general nutritional status appeared good, inasmuch as the patient had lost only three or four pounds. No liver function tests were performed (plasma proteins 7.4 Gm.%; hematocrit 49%). Owing to marked technical difficulties, operation was prolonged to four hours, and 500 cc. of whole blood were given on the operating table. A drop of 1.5 Gm.% in plasma proteins occurred in the first 48 hours. During this time, a massive atelectasis of the right lung developed, which was successfully treated by bronchial aspiration. On the second day 1000 cc. of whole blood were given, and an increase in protein concentration to 6.3 Gm.% followed. Feeding of amino-acids through a stomach tube, which was drawn through the anastomosis at the time of operation was started on the 5th postoperative day and another transfusion was administered two days later. The result of this therapy was eminently satisfactory, and a sustained high protein level was secured. A persistent elevation of the hematocrit reading despite absence of any clinical evidence of dehydration was an interesting finding.

Case 12.—F. R., Hosp. No. 89683. Benign pyloric obstruction. Gastro-enterostomy. This patient was considered a good operative risk and classified in Subgroup I (plasma proteins 7.0 Gm.%; hematocrit 44%; hippuric acid excretion 0.80 Gm.). Liver function was within normal limits. The operative procedure was easily and quickly performed

and 500 cc. of blood administered. The protein levels remained fairly stationary for the first week, but during this time the patient took very little food and was unable to tolerate amino-acids by mouth. Thereafter the proteins dropped considerably and reached 5.9 Gm.% on the 16th day. At this point, adequate feedings were satisfactorily instituted and a prompt response obtained. This case illustrates, again, the lack of protein reserves in patients with gastro-intestinal disturbances.

Case 13.—J. G., Hosp. No. 88423. Chronic obstructing duodenal ulcer. Gastro-enterostomy. This case is included to demonstrate the value of proper therapy. Intensive preoperative therapy with amino-acids by mouth and a high protein diet was instituted to replenish the protein reserve. The preoperative plasma protein level was 6.4 Gm.%, and the hematocrit was 40%. At operation, a transfusion of 600 cc. of blood was administered. A slight drop in proteins was observed, but this figure is misleading, inasmuch as marked hemoconcentration was present. Nevertheless, with amino-acid therapy through an indwelling tube, started on the 3rd postoperative day, a prompt rise in the proteins to a level above the preoperative figure was secured and maintained. Feedings by mouth were started on the 6th day, and the tube withdrawn.

Comment.—It became apparent to us that practically all patients with a long-standing gastro-intestinal disorder suffered depletion of their protein reserves in spite of normal plasma protein levels. Occasionally liver function was subnormal, probably as a result of malnutrition due to a deficient diet. In these patients a determined effort must be made to build up the protein reserve before operation and sustain this reserve after operation by transfusion and an easily assimilable protein diet. Neglect of these precautions was responsible for nutritional edema in two of our cases and contributed to a stormy and prolonged postoperative course in others. Feeding of amino-acids through an indwelling tube, which is drawn through the anastomotic stoma at the time of operation, can be started on the third or fourth postoperative day and serves admirably to maintain the protein level. When blood or plasma is not readily available this treatment is of tremendous value.

Case 14.—G. P. Hosp. No. 89360. Carcinoma of the breast. Radical mastectomy. The effect of excessive blood loss at operation is well illustrated by this case. The preoperative status was perfectly normal except for a carcinoma of the breast (plasma proteins 7.35 Gm.%; hematocrit 37%). The operation lasted one hour and fifty minutes, and blood loss was thought to be marked. A decline of 1.3 Gm.% in the plasma proteins occurred, but was fairly rapidly restored. The capacity of the average patient to replenish proteins lost as a result of hemorrhage is excellent.

Case 15.—G. K., Hosp. No. 88018. Ruptured peptic ulcer. Closure of perforation. Operation was performed immediately after admission, at which time the plasma proteins were 6.1 Gm.%, and the hematocrit 42%. This low level of plasma proteins was undoubtedly due to the moderate degree of shock following perforation of the ulcer. A further decline of 0.65 Gm.% was observed postoperatively, but within five days the proteins attained a level of 6.9 Gm.%, which was probably the normal figure. The convalescence of this patient was uneventful.

Case 16.—J. E., Hosp. No. 88206. Charcot hip. Arthrodesis. The preoperative figures were normal (plasma proteins 7.2 Gm.%; hematocrit 46%). The operation was extremely shocking and blood loss was great. A transfusion of 500 cc. at the time of operation was not sufficient to prevent the combined effects of shock and hemorrhage from lowering the protein level 1.6 Gm.%. Two subsequent transfusions were administered, but recovery was slow, and after 18 days the proteins had only reached 6.8 Gm.%. Obviously, further therapy with transfusions should have been administered,

Comment.—The relative effects of shock, hemorrhage, and both shock and hemorrhage together, are illustrated by the three preceding cases. Simple hemorrhage produces an effect which can be remedied fairly quickly. Shock, unaccompanied by hemorrhage, and insufficient in itself to cause irreversible changes, can also be rapidly balanced. When, however, both occur simultaneously the effect on the protein levels is much more marked and prolonged and must be strenuously treated without delay. Therefore, before starting operations which are known to be productive of shock and hemorrhage, transfusions should be commenced and continued until the operation is completed.

Case 17.—R. K., Hosp. No. 88563. Bleeding uterine fibroids. Hysterectomy. This patient had a severe secondary anemia as a result of repeated hemorrhages. The hematocrit was low, but the proteins were normal (plasma proteins 7.2 Gm.%; hematocrit 28%). A transfusion was given during the operation, but the protein concentration dropped 1.1 Gm.%, nevertheless. Another transfusion was given on the 3rd post-operative day, and thereafter the hematocrit and protein values returned to normal. This case illustrates the effect of severe anemia on the postoperative decline of plasma proteins. An operation which ordinarily causes but slight depletion of the proteins, was responsible for a significant loss in this patient, despite a transfusion of 500 cc. of whole blood.

Case 18.—R. S., Hosp. No. 87996. Uterine fibroids. Postoperative intestinal obstruction secondary to carcinoma of the sigmoid. Hysterectomy. Cecostomy. Pre-operative: Plasma proteins 6.8 Gm.%; hematocrit 42%. A simple hysterectomy was performed upon this patient, and a very slight immediate drop in proteins occurred. On the third postoperative day signs of intestinal obstruction developed, and these persisted. A marked decline in plasma proteins to 5.7 Gm.% was observed during this period. On the sixth day a cecostomy was performed and a transfusion administered. A slight response to the transfusion occurred but the proteins subsequently dropped to still lower levels (5.5 Gm.%) and for a period of 10 days the cecostomy functioned poorly. When the abdominal distension was finally overcome with a Miller-Abbott tube the plasma protein levels gradually returned to normal. The importance of repeated determinations of plasma protein levels in patients with actual or impending intestinal obstruction is well illustrated by this patient.

SUMMARY AND CONCLUSIONS

A significant decline in the plasma protein level was demonstrated in a considerable number of patients following surgical procedures. In a non-selective group of 215 patients, this decline was observed in 148, or 68.9 per cent. Our studies further indicated that a postoperative decline in plasma proteins was more common after certain types of operations. In this group were included operations upon the stomach and intestines, the biliary tract, the spine and large joints, and upon toxic thyroid disorders.

A combination of many factors influenced the extent and duration of the diminished protein concentration. Among the direct and immediate causes were blood loss, shock and anesthesia, while among the indirect causes were the nutritional status of the patient and extent of the protein reserves and the adequacy of liver function. The depreciation of plasma proteins as a result of blood loss and shock was usually of short duration and readily amenable to therapy, if it did not quickly and spontaneously return to

normal. When the protein reserves were exhausted or liver function was disturbed, the duration of protein depletion was prolonged and frequently the response to treatment was irregular.

The presence of subnormal hepatic function as demonstrated by the hippuric acid excretion test was a certain indicator that a postoperative protein decline would occur. Impairment of liver function was observed in 48 patients in this series, and a substantial diminution in the plasma protein concentration occurred in each case. Inasmuch as liver physiology is known to be disturbed frequently in certain surgical conditions of an extrahepatic nature, it is essential that liver function tests be performed routinely in these cases. Included in this category are patients with biliary disease, hyperthyroidism, severe gastro-intestinal disease associated with malnutrition, severe anemia, and carcinoma. The results of these tests should act as a guide for therapy.

The treatment of plasma protein depletion depends on the extent and duration, the amount of available protein reserves, and the adequacy of liver function. Since certain operations are known to be almost constantly associated with marked protein loss, the estimated loss should be replaced during the operation by blood or plasma transfusions. In patients with normal liver function and adequate protein reserves, this substitution will be the only treatment necessary and operation need not be delayed. If the protein reserves are thought to be exhausted postponement of the operation is indicated until the reserves can be restored. Dietary therapy is particularly valuable in these patients and should consist of a high protein diet which contains ample amounts of food with high contents of certain key amino-acids. If this diet cannot be administered amino-acids may be fed with satisfactory results.

In the group of patients with liver damage (Subgroup II) therapy should be directed to a restoration of normal hepatic function. It has been shown that the lipid content of the liver is an index of the ability of this organ to function adequately. A high lipid content is deleterious. Furthermore, there is evidence that proteins, and more particularly certain amino-acids such as methionine and cystine, have a great lipotropic effect; that is, they mobilize liver lipid and make it easily available for disposition. Therefore, in order to restore liver function to normal, ample amounts of selected proteins must be given along with sufficient carbohydrate to supply energy requirements. Plasma is a readily available and potent source of the necessary proteins and often proves efficacious when dietary therapy fails.

A study of the cases included in this series reveals that a proper therapeutic regimen is often neglected, and patients are operated upon before they are adequately prepared. We feel, that with proper preparation in the preoperative period, the extensive decline in the plasma proteins which were exhibited by these cases could be prevented frequently. Routine determinations of liver function should be made on all patients about to undergo major surgical procedures, and when possible, operation should be delayed until

restoration of adequate liver function is accomplished. Careful supervision of the diet and the more frequent use of plasma transfusions for their nutritional effect would enable most patients to avoid the threatened hypoproteinemia associated with the operations under discussion. Recently, by applying the therapy outlined above, we have been able to prevent, or greatly minimize, these declines in plasma protein concentration.

We are indebted to Mr. H. M. C. Luykx, Instructor in Preventive Medicine, New York University College of Medicine, who carried out the statistical analysis included in this work.

We wish to express our appreciation to Miss Fanny Davis who graciously volunteered her services and performed the many exacting laboratory determinations required by this study.

REFERENCES

- ¹ Whipple, G. H.: Blood Plasma Proteins. Editorial. *Surg. Gynec. & Obst.*, **73**, 886, 1941.
- ² Casten, D., and Bodenheimer, M.: The Problem of Hypoproteinemia in Surgical Patients. *Surg. Gynec. & Obst.*, **72**, 178, 1941.
- ³ Ravdin, I. S., Stengel, A., Jr., and Prushankin, M.: The Control of Hypoproteinemia in Surgical Patients. *J. A. M. A.*, **114**, 107, 1940.
- ⁴ Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema. *Arch. Surg.*, **27**, 159, 1933.
- ⁵ Quick, A. J.: Conjugation of Benzoic Acid with Glycine: A Test of Liver Function. *Proc. Soc. Exper. Biol. & Med.*, **29**, 1204, 1932.
- ⁶ Bartels, E. C., and Perkin, H. J.: Liver Function in Hyperthyroidism as determined by the Hippuric Acid Test. *New England J. Med.*, **216**, 1051, 1937.
- ⁷ Snell, A. M., and Plunkett, J. E.: The Hippuric Acid Test for Hepatic Function; Its Relation to Other Tests in General Use. *Am. J. Digest. Dis. & Nutrition*, **2**, 716, 1935.
- ⁸ Boyce, F. F., and McPetridge, E. M.: Studies of Hepatic Function by the Quick Hippuric Acid Test. *Arch. Surg.*, **37**, 401, 1938.
- ⁹ Collier, F. A., and Maddock, W. G.: Dehydration Attendant on Surgical Operations. *J. A. M. A.*, **99**, 875, 1932.
- ¹⁰ Veal, J. R., and Van Werden, B. deK.: Mortality of Spinal Analgesia Based on Analysis of 30 Immediate Fatalities in a Series of 33,811 Cases. *Am. J. Surg.*, **34**, 606, 1936.
- ¹¹ Johansen, A. H.: Hypoproteinemia. *Acta Path. et Microb. Scand.*, supp. **37**, 272, 1938.
- ¹² Thompson, W. H., McQuarrie, I., and Bell, E. T.: Edema Associated with Hypogenesis of Serum Proteins and Atrophic Changes in the Liver: with Studies of Water and Mineral Exchanges. *J. Pediat.*, **9**, 604, 1936.
- ¹³ Elman, R.: Acute Hypoproteinemia Following a Single Severe Hemorrhage in the Fasting Dog. *Amer. J. Physiol.*, **128**, 332, 1940.
- ¹⁴ Kerr, W. J., Hurwitz, S. H., and Whipple, G. H.: Regeneration of Blood Proteins. *Am. J. Phys.*, **47**, 356, 370, 379, 1918.
- ¹⁵ Smith, H. P., Belt, A. E., and Whipple, G. H.: Rapid Blood Plasma Depletion and Curve of Regeneration. *Am. J. Phys.*, **52**, 54, 1920.
- ¹⁶ Cutting, W. C., and Cutter, R. D.: Plasma Proteins Regeneration after Bleeding in the Rat. *Am. J. Physiol.*, **114**, 204, 1935.
- ¹⁷ Weech, A. A.: The Significance of the Albumin Fraction of the Serum. Harvey Lecture, *Bull. New York Acad. Med.*, **15**, 63, 1939.

PLASMA PROTEIN VARIATIONS

- 18 Madden, S. C., Noehren, W. A., Waraich, G. S., and Whipple, G. H.: Blood Plasma Protein Production as Influenced by Amino-acids. *J. Exper. Med.*, **69**, 721, 1939.
- 19 Miller, L. L., Ross, J. F., and Whipple, G. H.: Methionine and Cystine, Specific Protein Factors Preventing Chloroform Injury in Protein Depleted Dogs. *Am. J. Med. Sc.*, **200**, 739, 1940.
- 20 Goldschmidt, S., Vars, H. M., and Ravdin, I. S.: Influence of Foodstuffs upon Susceptibility of Liver to Injury by Chloroform and Probable Mechanism of their Action. *Clin. Invest.*, **18**, 277, 1939.
- 21 Smith, M. I.: Chronic Endemic Selenium Poisoning. *J. A. M. A.*, **116**, 562, 1941.
- 22 Moise, T. S., and Smith, A. H.: Diet and Tissue Growth. I. The Regeneration of Liver Tissue on Various Adequate Diets. *J. Exp. Med.*, **40**, 13, 1924.
- 23 Messinger, W. J., and Hawkins, W. B.: Arsphenamine Liver Injury Modified by Diet. *Am. J. M. Sc.*, **199**, 216, 1940.
- 24 Perlman, I., Stillman, N., and Chaikoff, I. L.: Radioactive Phosphorus as Indicator of Phospholipid Metabolism: Further Observations on Effect of Amino-acids in Phospholipid Activity of Liver. *J. Biol. Chem.*, **135**, 359, 1940.
- 25 Channon, H. J., and Wilkinson, H.: Protein and the Dietary Production of Fatty Livers. *Biochem. J.*, **29**, 350, 1935.
- 26 Tucker, H. F., and Eckstein, H. C.: The Effect of Supplementary Methionine and Cystine on the Production of Fatty Livers by Diet. *J. Biol. Chem.*, **121**, 479, 1937.
- 27 Connor, C. L.: Etiology and Pathogenesis of Alcoholic Cirrhosis of the Liver. *J. A. M. A.*, **112**, 387, 1939.
- 28 Montgomery, M. L., Entenman, C., and Chaikoff, I. L.: Liver Lipids of Dogs Subjected to Ligation of External Pancreatic Ducts. *J. Biol. Chem.*, **128**, 387, 1939.
- 29 Gyorgy, P., and Goldblatt, H.: Choline as a Member of Vitamin B₂ Complex. *J. Exper. Med.*, **72**, 1, 1940.
- 30 Bollman, J. L., and Mann, F. C.: Influence of Liver in Formation and Destruction of Bile Salts. *Am. J. Physiol.*, **116**, 214, 1936.
- 31 Schmidt, C. R., Walsh, W. S., and Chesky, V. E.: Liver Insufficiency in Toxic Goiter and Its Treatment. *Surg. Gynec. & Obst.*, **73**, 502, 1941.
- 32 Corey, E. L., and Britton, S. W.: Glycogen Levels in the Isolated Liver Perfused with Cortico-adrenal Extract, Insulin, etc. *Am. J. Physiol.*, **131**, 783, 1941.
- 33 Althausen, T. L.: Effects of the Administration of Glucose on the Glycogen Content of Normal and Experimentally Damaged Livers. *Ann. Int. Med.*, **6**, 193, 1932.
- 34 Wells, H. G.: Chemical Pathology, Ed. 5., W. B. Saunders Co., Philadelphia, pp. 20 and 481, 1925.
- 35 Scudder, J.: Shock: Blood Studies as a Guide to Therapy. J. B. Lippincott Co., Philadelphia, 1940.

CARCINOMA OF THE GUM

LT. COMDR. GEORGE S. JOHNSON, U.S.N.R., AND ROLLIN A. DANIEL, JR., M.D.
NASHVILLE, TENN.

FROM THE DEPARTMENT OF SURGERY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

SQUAMOUS CELL CARCINOMA arising in the buccal mucosa which covers the alveolar margin differs completely in its behavior from similar neoplasms which arise from other areas in the mouth and pharynx. The primary lesion is, from its origin, in close proximity to bone, and invasion of the bone occurs very early. It invades the bone widely while the visible area of ulceration remains small and sometimes innocent in appearance. The destruction of bone by the neoplasm and by infection which follows it give rise to pain. Unlike malignant disease in other areas in the body, pain may be a fairly early evidence of the disease, and the surgeon is consulted in many cases where the disease involves a small part of the soft tissues and is otherwise contained within the rigid and limiting structure of the jaw. This particularly applies to the cancer which arises on the lower alveolus and invades the mandible. This communication is concerned with the establishment of this lesion as an entity and with the treatment of cancer of the lower alveolus based upon knowledge of its usual mode of spread.

The term cancer of the gum has recently been applied to this lesion by Martin.¹ "Cancer of the jaw" or "carcinoma of the mandible" have been most frequently applied in the past, and these terms have been used to include carcinoma arising anywhere in the buccal mucosa and secondarily invading the mandible. New,^{2,3} in recent articles on the treatment of oral carcinoma, speaks of epithelioma of the lower jaw which "may originate in a previous papillary leukoplakia or the first symptoms may be a loosening of a tooth, starting in the body of the jaw." Probably squamous cell carcinoma and adamantinoma are grouped together, treatment of the lesions being disposed of by the simple statement that thorough destruction of all precancerous and malignant lesions with surgical diathermy gives the best chance of permanently getting rid of the trouble. As opposed to numerous reports on the treatment of oral cancer in which carcinoma of the lower alveolus is considered lightly, or not at all, other authors have set it aside as a problem more difficult to treat than other lesions of the mouth. Gardham⁴ calls attention to the extreme degree of malignancy usually present, and states that with five personal cases the longest survival period is two years. Resection of the mandible and primary bone graft was performed in this case. Blair, Brown and Byars⁵ called attention several years ago to the frequent need for complete destruction of the mandible following the use of radium in lethal doses, and advised against radiation of the bone, even where its use is effective in the soft tissues Shaw,⁶ and Ehrlich,⁷

CARCINOMA OF GUM

have discussed at length necrosis of bone as related to the use of radiation therapy, and both report the rare incidence of cures but do not suggest that other forms of therapy might be practiced in an effort to improve the rate of cure and to add to the comfort of patients. Albright,⁸ in 1935, published a complete review of the recent literature pertaining to the accepted methods of treatment of oral carcinoma, and stated that radiation here offers little. Primary destruction or excision without preliminary radiation is not sug-

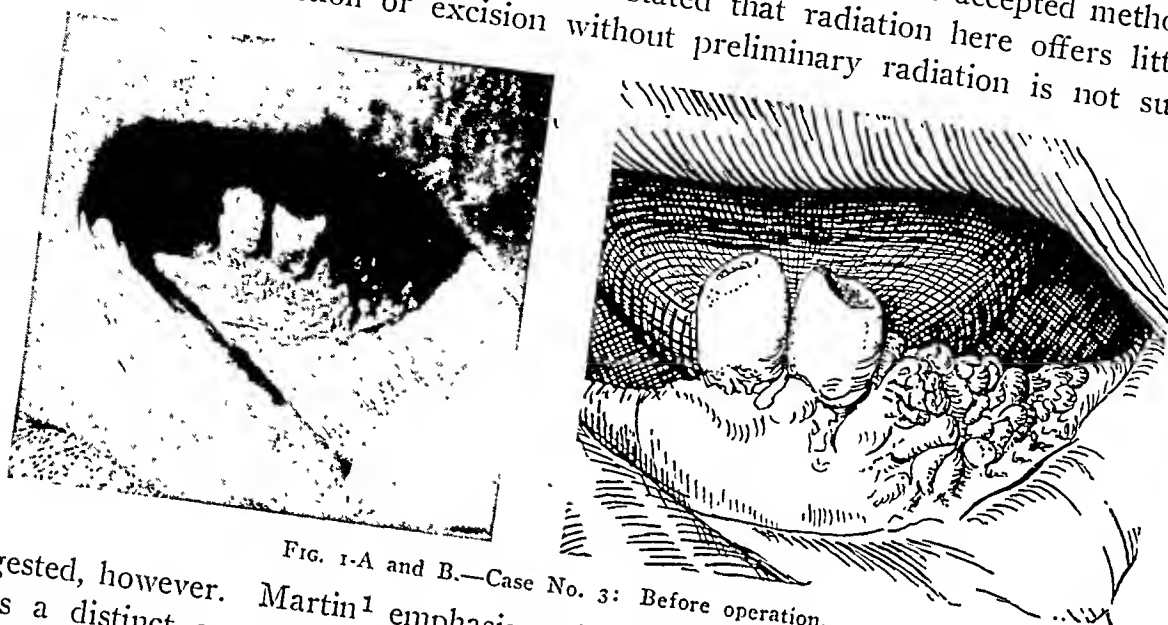


FIG. 1-A and B.—Case No. 3: Before operation.

gested, however. Martin¹ emphasizes the importance of alveolar carcinoma as a distinct anatomic form of intra-oral cancer, and states that it has received less attention than its relative frequency merits. As regards treatment, Martin states that "radiation (x-ray) therapy is the most useful and suitable method of treatment, since in the average case the growth in the gum is situated posteriorly, is over three centimeters in diameter, and involves at least one neighboring relatively inoperable structure." He advises the use of surgical excision in only the very earliest superficial lesions and employs roentgenotherapy by means of a carefully centered metal cylinder, through the open mouth. There were 57 malignant growths of the lower gum (about 95 per cent of which were squamous cell carcinoma), 15, or 26 per cent, of which are living without evidence of recurrence five years after treatment. About one-fourth of the patients treated by roentgenotherapy subsequently developed radio-osteomyelitis, with some loss of bone. These results are superior to others which have been reported, and are important also because only those lesions which originate in the buccal mucosa which overlies the alveolus are included.

THE TREATMENT OF CARCINOMA OF THE LOWER GUM AT THE VANDERBILT UNIVERSITY HOSPITAL

Prior to 1933 all cases of carcinoma of the gum seen in this clinic were treated either by roentgenotherapy or by radium, and no cures were obtained. Since 1933 cautery excision of the mandible, performed in much the same manner as was described by Bloodgood,⁹ and more recently by Blair, Moore and Byars,¹⁰ has been advised whenever it was thought that

the lesion might possibly be completely excised. The operative procedure has in most cases been supplemented by roentgenotherapy over the neck, but in no case which was thought to be operable was radiation of the primary lesion advised. At the time of operation the prime consideration has been eradication of the neoplasm. We believe that the fear of unsightly facial defects frequently influences the surgeon to perform limited intra-oral operations, as well as in the application of roentgenotherapy in empiric doses which are inadequate to destroy carcinoma which is growing in the mandible. Such procedures, carried out in patients with early lesions, are often worse than worthless, since longevity is not usually increased and the patient is subjected to the discomfort attending these forms of treatment.



FIG 2—Case No 3. Roentgenogram before operation.

Since 1933 there have been 111 patients observed with squamous cell carcinoma of the buccal mucosa and the lower lip in the Vanderbilt University Hospital. Fifty-nine of these began in the mucous membrane of the mouth itself (excluding the lip and the pharynx). Thirty, or 51 per cent of these growths apparently originated in the gum. Two arose in the gum of the upper alveolus, and 28, or 47.5 per cent, of these lesions began as an ulcer on the lower alveolar margin.

Four years have now elapsed since 23 patients with squamous cell carcinoma of the lower gum were first observed. Twelve of these patients were operated upon. A summary of the results in these cases is shown in Table I. The outcome in the remaining 11 cases is presented in summary in Table II. The technic of operation was the same in all but two patients in Table I. In these cases (Nos. 2 and 5), destruction of the full thickness of mandible was purposely not accomplished and the continuity of the inferior portion of the mandibular arch was preserved following sequestration.

CARCINOMA OF GUM

TABLE I
OPERATION—CAUTERY RESECTION OF MANDIBLE

Case No.	Age	Color	Sex	Duration of Early Symptoms	Postoperative Roentgenotherapy to Neck	Time of Sequestration of Mandible	Alive and Well. Time Since Operation	Result		
								Time After Operation	Dead Time After Onset of Symptoms	Cause of Death
1.	38	W.	F.	Ulceration 6 mos. Pain 1 month.....	2700 R.	10 weeks		7 mos.	13 mos.	Recurrence
2.	56	W.	F.	Ulceration 2 mos. Pain 2 weeks.....	6600 R.	20 weeks	4 years			
3.	51	W.	M.	Ulceration and tumefaction following extraction 3 mos.†.....	3280 R.	14 weeks	5½ years			
4.	57	W.	F.	Ulceration found by dentist 3 mos.†.....	6000 R.	8 weeks		11 mos.	14 mos.	Recurrence
5.	57	C.	M.	Ulceration 2 mos.....	1360 R.	8 weeks		12 hrs.		Cerebral accident (?)
6.	54	W.	M.	Ulceration 4 mos. Pain 1 month.....	None		6½ years			
7.	40	W.	F.	Soreness of jaw 12 mos. Bleeding 2 mos.....	3600 R.	20 weeks	5 years			
8.	73	W.	M.	Pain 4 mos. Ulceration about 24 mos.....	800 R.	16 weeks		10 mos.	14 mos.	Recurrence
9.*	77	W.	M.	Ulceration 6 mos. Soreness 3 mos.....	4500 R.	18 weeks		24 mos.	30 mos.	Recurrence
10.	57	C.	M.	Ulceration 5 yrs.† Pain 2 mos.....	6600 R.	12 weeks	4 years			
11.	74	W.	M.	Ulceration 5 mos. Pain 4 mos.....	6200 R.	16 weeks		3 years		Senility. No Recurrence
12.	36	W.	M.	Ulceration 2 yrs.† Pain 4 mos.....	None	12 weeks	4 years			

*9000 R. units, low voltage roentgenotherapy, using intra-oral cone, completed two months before operation (given elsewhere by competent Radiologic Clinic).

†Areas of ulceration failed to heal following tooth extractions.

TABLE II
OPERATION NOT PERFORMED

Case No.	Age	Color	Sex	Duration of Early Symptoms	Reason Operation Not Performed	Treatment	Duration of Life After First Appearance of Symptoms
13.	49	W.	M.	Ulceration 8 mos. Pain about 7-8 mos.....	Far advanced	Superficial X-ray (elsewhere)	10 mos.
14.	65	W.	M.	Ulceration 8 mos. Pain 3-4 mos.	Far advanced	None	12 mos.
15.	61	W.	F.	Ulceration and pain 12 mos....	Far advanced	X-ray refused	13 mos.
16.	53	W.	F.	Pain and ulceration 3 mos.....	Far advanced	X-ray 3600 R.	5 mos.
17.*	60	W.	M.	Pain and persistent ulcer following tooth extraction 4 mos.....	Refused	None	17 mos.
18.†	53	W.	M.	Ulceration and pain 6 mos.....	Far advanced	Radon: 7680 mc. hrs. (elsewhere). X-ray 6900 R.	17 mos.
19.†	51	W.	M.	Ulceration and pain 11 mos....	Far advanced	X-ray 2700 R.	17 mos.
20.*	46	W.	F.	Ulceration 7 mos. Pain 3-4 mos.	Refused	X-ray 4000 R.	16 mos.
21.*	58	W.	F.	Pain and ulceration 5 mos.....	Refused	X-ray (elsewhere)	13 mos.
22.*	74	W.	M.	Ulceration 3 mos. Pain 2 mos.	Refused	X-ray 2200 R.	26 mos.
23.*	61	W.	M.	Pain 3 mos. Ulceration 2 mos.	Refused	X-ray (elsewhere)	7 mos.

*Considered to be operable when first examined by us. Patient refused operation.

†Local removal by cauterization and application of radium performed elsewhere before patient first seen at Vanderbilt Hospital.

TECHNIC OF OPERATION

An incision is made beginning at about the symphysis of the mandible and is extended outward and down to the level of the hyoid bone under the body of the mandible. The incision there curves upward to extend slightly above the angle of the mandible. The skin and subcutaneous tissue of the flap are elevated, the incision being extended through the labial mucous membrane into the mouth. A suprahyoid neck dissection is then carried out, the incision being carried entirely through the muscles and mucous membrane of the floor of the mouth and care being taken to carry the incision through healthy tissue well away from the edges of the growth. The lip and skin flap are retracted upward, and moist saline packs are applied to cover the soft tissue of the neck, face and the mouth. The soft tissues adherent to the body of the mandible are excised, usually with the electrocautery. Hot soldering irons are used to cauterize the mandible and are applied for a sufficient length of time to assure destruction of the whole thickness of the bone and all of its attached soft parts. The mandible is not divided. The external skin flap is then brought back down into place and a few interrupted sutures are placed in the ends of the wound, its central aspect being left open. Flat packs of gauze are placed in the defect, against both sides of the mandible and a firm external dressing is applied.

A tube is frequently passed into the stomach, through the nose, for feeding purposes.

Chloroform anesthesia has been used in all cases, administered through an endotracheal catheter.

PREOPERATIVE AND POSTOPERATIVE MANAGEMENT

All patients are given high carbohydrate, high protein diets for two days before operation, with added frequent feedings of sugar. An adequate intake of fluid before operation is assured.

As soon as the patient is fully reacted, he is allowed to assume a sitting or semisitting posture. Feeding is usually accomplished during the first few days by means of the inlying stomach tube. All patients are gotten out of bed as soon as possible following operation and are encouraged to increase their activity as rapidly as can be tolerated.

Drainage from the wounds becomes fairly profuse and of a foul nature during the second week after operation. Following this period, during which slough of necrotic soft tissue occurs, the wound rapidly becomes cleaner, the fistula smaller and drainage less marked. Care is taken in the instruction of patients regarding the frequent taking of liquid and soft foods, and on discharge from the hospital the patient is given a list containing various essential foods to be included in his diet. Dressings are changed as frequently as may be desirable at home.

Separation and discharge of the dead mandible occurs in from two to five months following operation (average time 14 weeks). In most instances the bone has been easily lifted out of the wound during a regular follow-up

CARCINOMA OF GUM



FIG. 3-A

Fig 3.—Case No. 3: A and B Appearance of sequestrum three and one-half months after operation.



FIG. 3-B

visit to the Tumor Clinic. Following sequestration, the opposite mandible swings a little toward the midline, and the fistula becomes somewhat smaller and quite clean. The patient is readmitted to the hospital a few weeks later and closure of the oral fistula is accomplished.

The appearance of the patient following closure of the fistula has been satisfactory in most cases. If there is no recurrence of the lesion after a year, plastic procedures may be carried out for the restoration of the continuity of the mandibular arch and improvement in the cosmetic results. In most cases these procedures will be refused by the patient.

The functional result is equally satisfactory. Speech is not seriously interfered with and the mastication of soft foods can be accomplished.



FIG. 4.—Case No. 3: Roentgenogram three and one-half months after operation, just before removal of mandible.

DISCUSSION

The earliest symptom in most cases has been ulceration of the gum. This has been followed within a few weeks by soreness and then by pain in the jaw. All but four of the 23 patients presented themselves for examination after the onset of pain and 17 patients (74 per cent) were advised to have operation.

The average duration of symptoms in the group of patients operated upon was six and one-half months. In those who were inoperable the average duration of symptoms at the time advice was sought was seven and three-fourths months.

Five patients refused operation. In one of these cases no treatment was instituted. This patient lived for 17 months after the first symptoms. Roentgenotherapy was employed in the remaining four cases, and their

CARCINOMA OF GUM



FIG. 5.—Case No. 3: Roentgenogram following removal of mandible and closure of oral fistula, nine months after operation.

average duration of life was 15.5 months, one patient living for 26 months after the lesion was first noticed. The average duration of life after onset in the entire group not operated upon (Table II) was 14 months. The average duration of life in four patients who were operated upon but who died of recurrence was 17.7 months after appearance of first symptom and 13 months following operation. Six patients are alive and well

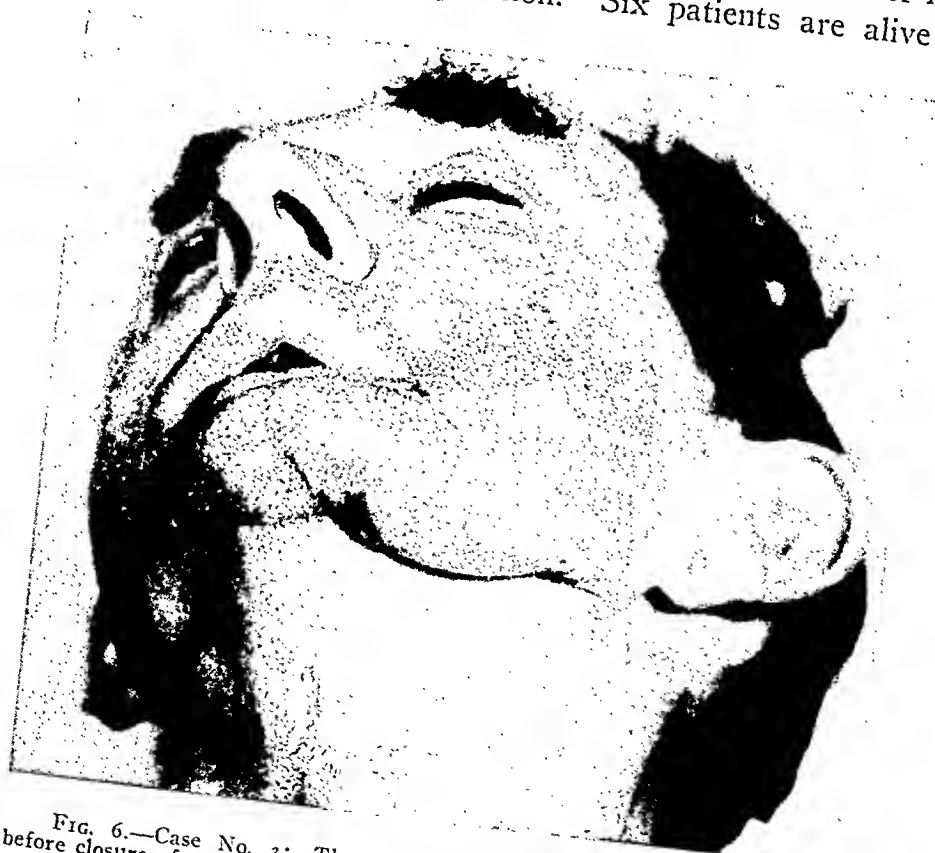


FIG. 6.—Case No. 3: Three months after removal of mandible, just before closure of oral fistula. Note midline position of the chin.

four years or more after operation. The average duration of life following onset of symptoms is four years and 10 months.

Ages of the patients, when first seen, ranged from 36 to 77. Three patients subjected to operation were more than 70 years old.

There were 15 males and eight females in the entire group of patients. Seven patients had adentia. Six of these had badly fitting lower dentures and were conscious of irritation of the lower gum caused by "rubbing" of the plate. The other patient (No. 9, Table I) had had adentia for 25 years and had never worn false teeth. In all of the patients in whom there were remaining teeth, dental caries were numerous and the gums were retracted and badly infected.



FIG. 7-A.—Case No. 9. Before operation.

There was one operative death (No. 5). This patient lived for 12 hours after operation and did not regain consciousness. Autopsy was not performed. This is an operative mortality rate of 8.33 per cent.

Six patients operated upon have lived for four years or longer without evidence of recurrence. This is a survival rate of 50 per cent. One other patient (No. 11), who was 74 years old when operation was performed, died in a State Hospital for mental diseases three years after operation. There was no evidence of recurrence at the time of his death. Four patients (33.3 per cent) died of recurrence of malignant disease.

Protracted external roentgenotherapy was given over the neck following operation in all cases who survived except one. The total dosage of radiation therapy employed in each case is given in Tables I and II.

Patient No. 9 was treated intensively with protracted intra-oral roentgenotherapy, administered through an intra-oral cone, before he was seen by us. The rate of growth of the neoplasm was probably influenced by this therapy but the patient was sent to this clinic by the roentgenologists who treated him because they observed evidences of continued growth. Resection of the mandible was performed but the patient ultimately died of recurrence of the growth and metastases.

Another patient (No. 18) received very intensive interstitial radiation (radon: 7680 millicurie hours) and when he was seen in the Vanderbilt University Hospital he had extensive invasion of the mandible, the floor of the mouth and the tongue, and the neck. 6900 R units of roentgenotherapy were given, and the patient died 17 months after the onset of symptoms.

SUMMARY

1. Squamous cell carcinoma of the lower gum (alveolar epithelial margin) constitutes almost one-half of malignant growths of the buccal mucosa.

CARCINOMA OF GUM

2. Early erosion of the cortex of the mandible takes place and subsequent widespread invasion of the mandible occurs while the disease is still limited to a small area in the soft tissues.
3. In recent years, because of the fear of mutilating facial operations and the ease of application of radiation therapy, surgical excision of the mandible

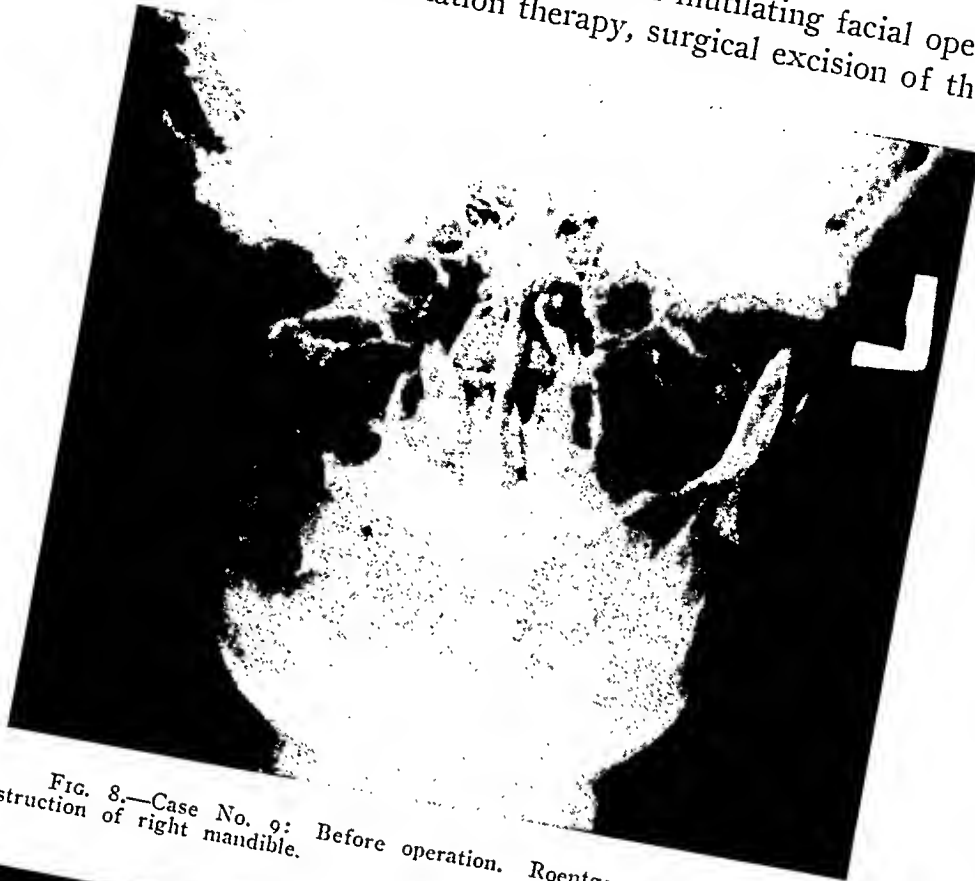


FIG. 8.—Case No. 9: Before operation. Roentgenogram showing destruction of right mandible.



FIG. 9.—Case No. 9: Eight months after operation and three months after closure of oral fistula. has been largely abandoned in favor of radiation therapy. The treatment of squamous cell carcinoma of the gum has been disappointing, on the whole.

4. Eradication of the disease can be accomplished in a relatively large number of patients by wide, *en bloc* excision of the body of the mandible and its adjacent soft tissues.

REFERENCES

- ¹ Martin, Hayes: Cancer of the Gums (Gingivae). *Am. J. Surg.*, **54**, 769, 1941.
- ² New, G. B.: Malignant Disease of the Mouth and Accessory Structures. *Am. J. Surg.*, **30**, 46, 1935.
- ³ *Idem*: Cancer of the Tongue and Lower Jaw. *Tr. Am. Laryng., Rhin. and Otol. Soc.*, **41**, 610, 1935.
- ⁴ Gardham, A. J.: *Lancet*, **1**, 677, March 25, 1939.
- ⁵ Blair, V. P., Brown, J. B., and Byars, L. T.: Cancer of the Cheek and Neighboring Bone. *Am. J. Surg.*, **30**, 250, 1935.
- ⁶ Shaw, J. J. M.: Cancer of the Mouth and Jaws. *Edinburg Med. J.*, **46**, 639, 1939.
- ⁷ Ehrlich, D. E.: Bone Necrosis in Intra-oral Cancer. *Arch. Phys. Therapy*, **18**, 565, 1937.
- ⁸ Albright, H. L.: Carcinoma of the Mouth. *Radiology*, **25**, 24, 1935.
- ⁹ Bloodgood, J. C.: Oral Cancer. *J. Am. Dent. Asso.*, **20**, 1790, 1933.
- ¹⁰ Blair, V. P., Moore, S., and Byars, L. T.: Cancer of the Face and Mouth. C. V. Mosby Co., pp. 187-209, 1941.

RATE OF EPITHELIAL REGENERATION

A CLINICAL METHOD OF MEASUREMENT, AND THE EFFECT OF VARIOUS
AGENTS RECOMMENDED IN THE TREATMENT OF BURNS

BRADFORD CANNON, M.D., AND OLIVER COPE, M.D.

BOSTON, MASS.

FROM THE DEPARTMENT OF SURGERY, HARVARD MEDICAL SCHOOL, AND THE SURGICAL SERVICES,
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

For some years certain members of the staff of this hospital have felt that the tanning methods in vogue for the treatment of burns are injurious to viable epithelium. The burned surfaces treated with tannic acid or various dyes have not healed as rapidly as those treated with bland ointments. This apparent delay in wound healing has remained, however, but a clinical impression. In the burned patient there are factors, other than the substance applied locally, which influence the rate of healing, and the rôle played by each may be impossible to appraise.

In the first place, the deeper the burn, the slower the healing will be. No two burned areas can be considered of identical depth or degree, and there is no proven method of judging accurately, clinically, or microscopically, the extent to which the cells are damaged by the burn. Second, complications of the burn, infection and malnutrition, delay the eventual healing. The growth of organisms on the burned surface may destroy additional cells and retard regeneration of epithelium. Acute malnutrition with loss of protein reserves may occur as the result of plasma loss and infection; an adequate protein reserve is a requisite of cellular proliferation and wound healing.¹

The tannic acid treatment for burns was introduced by Davidson,² in 1928, at a time when the toxin theory of shock was popular. One of the arguments for its use was the concept that the tannic acid would coagulate, *in situ*, any tissue toxins produced in the burned cells and thus present or retard their absorption. Davidson felt that the tannic acid did not coagulate viable cells, but he had no objective method of measurement.

Tannic acid proved to have low bactericidal powers. Abscesses developed beneath the tannic eschar with too great frequency. In order to reduce the element of infection, Firor and Aldrich³ recommended gentian violet. Such dyes in high concentrations produce a supple eschar and abscesses beneath are less common.* The evaluation of dyes in contrast to tannic acid has, incidentally, prompted attention to the rôle of infection in the late shock of burns.

Both tannic acid and dyes have represented improvements in the treat-

* Aldrich⁴ has developed a modification of the dye treatment with his triple dyes. For bactericidal purposes, they have certain advantages over gentian violet alone.

ment of burned patients, but it must be recalled that their recent introduction† has coincided with the understanding of protein and fluid therapy. The attention of those recommending tannic acid or dyes has been so riveted on fluid loss, toxins, or infection, that they have neglected the possible noxious effect of these substances upon the viable epithelium.

Reports have recently appeared from England questioning the innocence of tannic acid⁶ and the dyes.⁷ In this country, Dragstedt, *et al.*,⁸ and Koch,⁹ among others, have advocated other methods supposedly less injurious to the viable tissues. The evidence in these reports is based either upon clinical observation, or, in the case of the dyes, upon their influence on the growth of tissue cultures. Objectively controlled measurement of the effect of tannic acid, dyes, and other substances upon the regeneration of human epithelium *in situ* is lacking.

Various substances recommended for the treatment of burned surfaces have been assayed by a simple method which judges, in the human being, the rate of healing of skin wounds. This communication presents a description of the method and the results so far obtained.

METHODS

The effect of substances upon the rate of epithelial regeneration has been measured in the human, using the donor area from which a graft of uniform thickness is cut. The donor area is subdivided into two or more portions, one of which is covered by a standard and the others by experimental preparations.

The patients used in this study required grafts of skin for various elective plastic procedures, not for burned surfaces of recent origin. The patients were healthy and otherwise normal. The diets given were adequate in protein and vitamins. No nutritional deficiencies were observed, but blood serum protein and vitamin levels were not determined. The convalescence of all patients during the hospital stay was uneventful.

The donor site chosen was usually their lateral or medial side of the thigh, the graft being cut longitudinally. No grafts were cut transversely around the thigh, since it is considered that the skin on the inside of the thigh is not comparable to that on the outside. Occasionally the abdomen, and once the posterior surface of the lower leg, were used. The donor surface chosen was normal; it contained no scar and no previous grafts had been removed from it.

The area was shaved and washed with soap, water, and alcohol, and wrapped in a sterile towel the night preceding operation. At operation, the area was painted with three per cent iodine solution and draped.

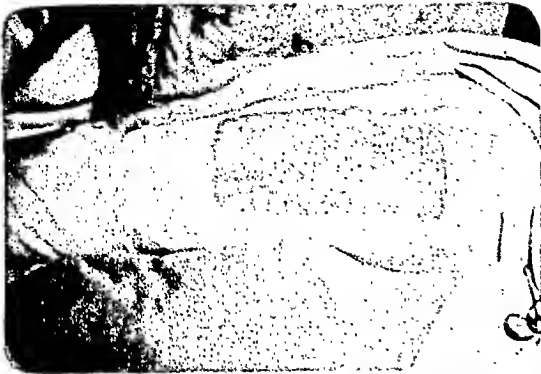
A skin graft of uniform thickness was removed by the dermatome.¹⁰ A standard depth of 0.012-inch was chosen. It is difficult to obtain a uniform cut with the knife set for a thinner graft. A thicker cut would penetrate

† Tannic acid was employed in Glasgow in the nineteenth century,⁵ as well as in the Orient far earlier.

A



B



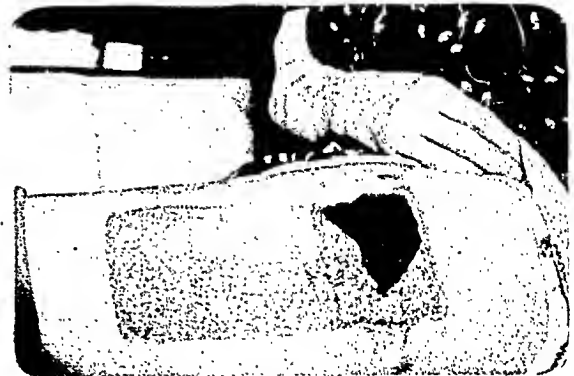
C



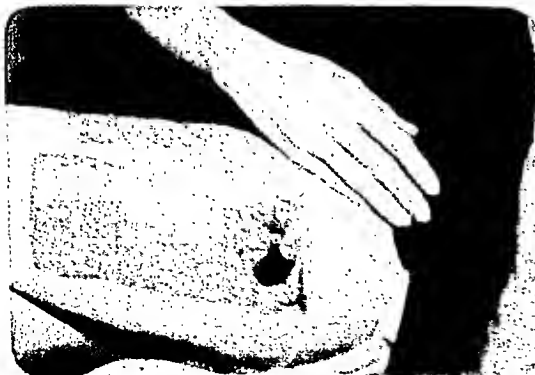
D



E



F



G

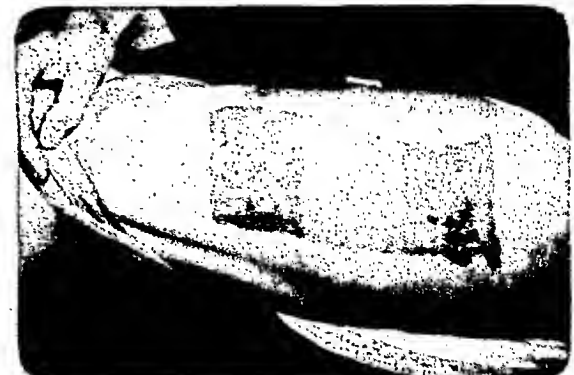


PLATE I.—A to G: Photographs of the donor site on the lateral aspect of the left thigh of Patient 8. The middle third of the donor site was used as the control portion and covered with boric ointment gauze. The proximal third (right side of photograph) was treated with triple dye. The distal third was treated with tannic acid. A: Skin before removal of graft. B: Donor site before application of agents. C: Fourth postoperative day. The adhesive strapping in the middle holds the boric dressing in place. D: Sixteenth postoperative day. The control area is healed. E: Twenty-sixth postoperative day. The tannic acid area is healed. F: Thirty-third postoperative day. In the triple dye area, part of the eschar is still adherent and there are several small areas not yet covered with epithelium. G: Sixty-first postoperative day. There are still unhealed portions of the triple dye area.

EPITHELIAL REGENERATION

too deeply into the dermis, decreasing the proportion of epithelium to connective tissue in the residual dermis; healing would, therefore, involve fibrous tissue as well as epithelial regeneration.

Aerobic and anaerobic cultures of the donor area were taken immediately after removing the graft in 12 of the early cases.

A fine-mesh gauze lightly impregnated with boric acid ointment* was the standard preparation applied to the control portion of the donor area. A firm dressing was applied over the boric acid ointment gauze, anchoring it securely, and isolating it from the experimental areas. If the donor area was of sufficient length, the middle third was used as the control portion, with an experimental portion above and below it; otherwise, the area was divided into two portions.

Healing was judged to have taken place when the wound became closed, that is when the surface was covered with intact epithelium, unbreakable by the trauma of ordinary activity. The reparative process continues beyond this point, but this stage of healing was chosen because it can be ascertained clinically. It is the stage at which a dressing can first be removed without causing bleeding.

The healing of the portions of a single donor site only were compared. Even in the same patient, donor sites in different areas of the body are not necessarily similar, since the thickness of the skin differs, and although the graft removed may be of the same depth, the residual dermis and the time required for healing may differ.

Colored photographs, as records, have been taken of the donor site at operation, and at intervals during the healing period (PLATE I).

EXPERIMENTS

The donor sites of 27 patients have been used. The effect upon healing of 14 substances was compared with that of boric acid ointment; nine of these were escharotics, the others ointments. The cultures taken of the donor area at operation in 12 cases showed a scant growth of nonpathogenic bacteria in six cases.

Tannic Acid.—A ten per cent solution of tannic acid, with an approximate pH of 2, was applied to nine cases (Table I). It was sprayed on with an atomizer, at 15-minute intervals, during the first few hours after the graft had been taken and was continued at half-hourly intervals until a firm eschar had formed. In most instances the bleeding from the raw surface continued after the first application of the tan. As this interfered with the formation of the eschar, it was gently sponged away and the spray repeated. A smooth, firm eschar resulted.

The tannic eschar was removed from 14 to 26 days after operation. In only Case 2 had healing occurred by the fourteenth day. In Case 5, the

*Boric acid ointment (boric acid, 10 per cent, in petrolatum) was chosen because it is ubiquitous, and experience suggests it to be relatively innocuous. The gauze used was No. 40- x 44-mesh.

TABLE I
Day on which Healing was Observed

Agent	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27
Boric acid ointment.....	14	14	13	16	12	14	11	14	13	9	10	10	9	13	13	9	10	10	9	9	10	10	14	9	9	11	12
Tannic acid.....	14+	14*	22+	18+	15	14+	15	26	15
Tannic acid and silver nitrate.....	14++	14*	22++	15
Gentian violet.....	18+	31+	26+	30+
Triple dye.....	50+	20+	61+
Fibrinogen, with boric acid ointment.....	9	10	10	18	9
dry gauze.....	13	11+
tannic acid.....	13	13
Triethanolamine-sulfadiazine.....	21	16
Triethanolamine-sulfadiazine, with methocel.....	11+
Pectinate:
Nickel and silver	10	14
Scarlet red ointment.....	10	11
Collagen membrane.....	9+
Sulfadiazine ointment (U. S. Government).....	9	11	12
Sulfadiazine ointment (Dixon's).....	14	38+

*Blood was not sponged away during tanning. The larger portion of the surface was healed at 14 days; in small areas the eschar was still adherent.
 +Healing not complete on specified day; actual date of healing not determined.
 —Dressing no longer adherent when first observed; healing, as defined, had occurred earlier.

EPITHELIAL REGENERATION

surface was healed over in 15 days; the longest time required was 26 days. The controls, on the other hand, were all healed when first examined, 11 to 16 days after operation. The boric acid gauze dressing was readily removed in all these cases, and it was suspected that the healing, as defined, had occurred earlier. In subsequent cases, therefore, the boric acid dressing was examined on the ninth or tenth day, and, indeed, healing was found to have occurred by this time. A greater discrepancy in the time of healing between the control and tannic acid areas presumably exists, therefore, than that recorded in the nine experiments in this group. It is concluded that tannic acid causes a delay in epithelial regeneration.

In keeping with this conclusion is the single observation (Case 2) in which patient the blood was not sponged from the surface of the donor site as the tannic acid was applied. Healing had taken place over the larger part of the area in 14 days, but portions of the eschar were still adherent. It is felt that the blood had formed a protective layer between the wound surface and the tannic acid, and that the eschar was formed in large part, of tanned blood.

Tannic Acid and Silver Nitrate.—Tannic acid, five per cent, and silver nitrate, five per cent, were applied to donor areas in four cases, either with an atomizer or by means of cotton sponges. The application was continued at regular intervals until a firm, dry eschar was formed, usually within 24 hours. The observation about the protective effect of the blood clotting on the raw surface was made again in Case 2. When the blood was removed during tanning, healing was the same, or slower than when tannic acid alone was used. Both eschars, tannic acid alone and with silver nitrate, were removed in Cases 1 and 3 before they were free, and healing was not only behind that of the control portion but was less advanced under the silver nitrate than that beneath the tannic acid alone.

Gentian Violet.—Gentian violet, two per cent, was sprayed on to the donor area of four cases. The dye stopped the bleeding from the surface quickly and the eschar formed more rapidly than with either of the tannic acid solutions. The healing of the areas was delayed. One patient was discharged from the hospital on the eighteenth day and another on the twenty-sixth day, each with an unhealed wound. The other two patients were kept in the hospital for 30 days, and the wounds still were not healed. The control portions of the wounds healed in periods comparable with those recorded in the tannic acid experiments.

*Triple Dye.** The triple dye mixture, two per cent, used in three cases, behaved much as the gentian violet alone—bleeding was stopped and the eschar formed rapidly. One patient, Case 7, was discharged on the twentieth postoperative day, with the eschar firmly attached. The eschar of the other two patients was removed on the twenty-sixth day and, since the healing was not complete, boric acid ointment gauze was applied, and the patients

* Triple dye formula: Crystal gentian violet 3.0, brilliant green 2.0, neutral acriflavine 2.0, two per cent solution.

discharged. The wounds were not completely healed on the fiftieth and sixty-first days. The control portion was healed in one case in 11 days, and in two, in 14 days.

Fibrinogen.—A powder of human fibrinogen, thrombin, five per cent sulfadiazine, and a phosphate buffer,[†] was tried on nine areas. This mixture was sprayed on the donor surface with a powder blower until there was a thick frosting. The fibrinogen clotted promptly but bleeding continued beneath the clot, forming blebs. When these blebs were ruptured, uncoagulated blood escaped. Because of the continued formation of the blebs and the fragility of the coagulum, a dressing was necessary for support. In five of the areas, boric acid ointment gauze was applied as a dressing over the fibrinogen. In two other cases, a dry fine-mesh gauze was placed directly over the fibrinogen. In the remaining two areas the fibrinogen surface was tanned with a ten per cent tannic acid solution and no dressing applied.

Three of the seven control portions were healed in nine days, two, in 10 days, and two, in less than 13 days.

In four of the areas with boric acid ointment gauze over fibrinogen, healing occurred in two, in nine days, and in two, in ten days. A thin coagulum separated the gauze from the new epithelial surface. In the fifth area, healing was delayed until the eighteenth day. In the two areas on which a dry, fine-mesh gauze was placed directly over the fibrinogen, healing was retarded until the eleventh and thirteenth days. In the two areas which were tanned, the eschar formed and dried rapidly, usually in less than eight hours. The blebs of blood continued to rupture during that time. The eschar was thin and, at first, soft and flexible. Later, it contracted, curled, broke and came off in pieces. Healing had occurred in both control and experimental surfaces in the two cases, when the dressing and eschar were removed on the thirteenth day.

*Triethanolamine-Sulfadiazine (Lederle).**—Sulfadiazine, five per cent, in triethanolamine,¹¹ was sprayed on a portion of the donor area of two cases. In one case, healing was not complete until the twenty-first day, the control portion having healed on the ninth day. In the second case, healing was complete on the sixteenth day; the control portion was healed by the fourteenth day.

Triethanolamine-Sulfadiazine with Methocel (Lederle).—Triethanolamine-sulfadiazine with methocel was applied in one case. There was considerable difficulty in developing a firm eschar. Some maceration occurred at the junction of the control area and the area treated with the eschar. Healing of the control area was complete in nine days, and most of the area treated with the escharotic in 11 days.

Pectinates.—Various pectinates have been recommended as coatings for wound surfaces.¹² The donor site of two cases was treated with a gel of

[†] The fibrinogen powder was furnished for clinical evaluation by Professor Edwin J. Cohn, and his associates.

* Formula: Sulfadiazine 2.5 per cent, triethanolamine 8.0 per cent, sodium benzoate 0.2 per cent, water q.s. 100 per cent.

EPITHELIAL REGENERATION

nickel and silver pectinate. Over each, a dry, fine-mesh gauze was applied, with a pressure dressing. Healing in one of these cases was complete on the tenth day and in the other on the fourteenth day. Both control areas were healed on the tenth day.

Scarlet Red Ointment.—Scarlet red ointment, five per cent, impregnated gauze, was used in two cases. Healing in these cases was complete on the tenth and eleventh days. Only one of these had a control area and the healing was complete on the same day.

Collagen.^{*}—Two sheets of pure collagen, one containing sulfadiazine, were applied to two areas in one case. Considerable blood collected beneath the pure collagen membrane, forming a crust in a few days. There was no significant bleeding beneath the collagen membrane containing the sulfadiazine. Healing of the control area and that with the collagen membrane containing the sulfadiazine was complete in nine days. The dry crust which formed beneath the pure collagen membrane became corrugated and healing of this surface was delayed.

Sulfadiazine Ointment, five per cent (Lederle—U. S. Government 175 H 14).—Sulfadiazine ointment, five per cent, made for the U. S. Government by Lederle, was used in three cases, a fine-mesh gauze being lightly impregnated with the ointment. In these cases healing occurred in 9, 11 and 12 days, respectively. The time of healing in the control areas was the same in each instance.

Sulfadiazine Ointment, five per cent (Lederle-Dixon 300 H 1194).—Dixon's ointment, with sulfadiazine, five per cent, was applied in two cases. Healing occurred in one case in 14 days; the control was healed in ten days. In the other case there was considerable maceration of the area, and healing was delayed for more than 38 days; the control area was healed in 11 days.

COMMENT

Two processes are involved in the healing of a surface wound; one is the proliferation of cells, the other contraction of the wound. The latter is accomplished by shrinkage of elastic elements in the tissues surrounding the wound and of the fibrin eschar which nature makes for such a wound. The wound created by the dermatome, set to cut a graft of uniform thickness, as described, heals primarily by cellular proliferation, with a minimum of contraction. (The area of the wound left by the dermatome remains constant during the healing). It is, therefore, a wound peculiarly suited to judging the effect of agents on epithelial growth.

The donor site is not comparable in many respects to the débrided surface of the second-degree burn. But control of the variables found in burns, such as depth of injury and infection, is so easy, using this standard wound, that it is suggested that any substance to be recommended for the local treatment of a burn should be evaluated by this simple, clinical method.

^{*} The purified collagen was prepared by Professor F. O. Schmitt, and his associates, at the Massachusetts Institute of Technology.

In this communication are reported delays in epithelial regeneration in donor areas after the application of certain chemical agents which have been recommended in the treatment of the burned surface. Admittedly, more than the single factor of epithelial regeneration enters into the choice of an agent for the treatment of a burned surface, and no attempt is made herein to evaluate other advantages or disadvantages of the various substances.

The discrepancy in healing time between the control and experimental areas is the more significant, in view of the surprising consistency in healing time of the control areas in the various patients. Such uniformity is not to be expected in unhealthy, depleted patients, or in those with endocrine disorders. It is, therefore, to be stressed that when using this method each patient must serve as his own control, and, indeed, that a portion of the same donor area, not that of an area in another part of the body must be used for the control.

SUMMARY AND CONCLUSION

The donor area from which a skin graft of uniform thickness has been cut with the dermatome offers a simple, clinical medium for judging the effect of substances upon the healing of an epithelial wound. Various agents recommended for the treatment of a débrided burn surface have been tested by applying them to the donor areas. Tannic acid, tannic acid and silver nitrate, gentian violet, the triple dyes, and triethanolamine solutions, all have been found to delay epithelial healing as compared with the control boric acid ointment.

REFERENCES

- ¹ Ravdin, I. S.: Hypoproteinemia and Its Relation to Surgical Problems. *ANNALS OF SURGERY*, 112, 576, 1940.
- ² Davidson, E. C.: Tannic Acid in the Treatment of Burns. *Surg., Gynec. & Obst.*, 41, 202, 1925.
- ³ Aldrich, R. H.: The Role of Infection in Burns: The Theory and Treatment, with Special Reference to Gentian Violet. *New England Jour. Med.*, 208, 299, 1933.
- ⁴ Aldrich, R. H.: Treatment of Burns with a Compound of Aniline Dyes. *New England Jour. Med.*, 217, 911, 1937.
- ⁵ Dunbar, J.: Review of Burn Cases Treated in the Glasgow Royal Infirmary During the Past 100 Years (1833-1933): With Some Observations on Present-Day Treatment. *Glasgow M. Jour.*, 122, 239, 1934.
- ⁶ Mowlem, R.: The Treatment of Burns. *Proc. Royal Soc. Med.*, 34, 221, 1941.
- ⁷ Jacoby, F., Medawar, P. B., and Willmer, E. N.: The Toxicity of Sulphonamide Drugs to Cells in Vitro. *Brit. Med. Jour.*, 2, 149, 1941.
- ⁸ Allan, J. G., Owens, F. M., Jr., Evans, B. H., and Dragstedt, L. R.: Sulfathiazole Ointment in the Treatment of Burns. *Arch. Surg.*, 44, 819, 1942.
- ⁹ Koch, S. L.: Treatment of Burns. *Bull. Am. Coll. Surg.*, 27, 106, 1942.
- ¹⁰ Padgett, E. C.: Calibrated Intermediate Skin Grafts. *Surg., Gynec. & Obst.*, 69, 799, 1939.
- ¹¹ Pickrell, K. L.: New Treatment for Burns: Preliminary Report. *Bull. Johns Hopkins Hosp.*, 69, 217, 1941.
- ¹² Norton, P. L.: The Effect of Pectin and Nickel Pectinate on the Healing of Granulating Wounds in Albino Rats. *Am. Jour. Surg.*, 56, 573, 1942.

INTRATHORACIC NEUROBLASTOMA

CASE REPORT

WALTER E. LEE, M.D., AND JOSEPH A. RITTER, M.D.

PHILADELPHIA, PA.

FROM THE DEPARTMENTS OF SURGERY AND PEDIATRICS, GRADUATE HOSPITAL, UNIVERSITY OF PENNSYLVANIA
PHILADELPHIA, PA.

TUMORS derived from embryonal neurogenic tissue are not uncommon in infancy and childhood. This neurogenic tissue, or sympathogonia, differentiates either into the sympathoblasts and sympathetic ganglion cells or the chromaffin cells of the adrenal medulla. Four types of tumors arise from these embryonal cells, the malignant sympathogonioma, the benign ganglioneuroma, the chromaffinoma of the adrenal medulla and the malignant neuroblastoma. The neuroblastoma is the most commonly encountered of these tumors in infancy and childhood. They vary both in size and shape from a small, smooth encapsulated mass to a large lobulated tumor and grow rapidly involving contiguous structures or metastasize through blood vessels and the lymph stream. The typical histologic appearance (Ladd and Gross¹) show the cells in a rosette pattern, with the cytoplasm concentrated in the center of the cell and the nuclei situated in the periphery. Fine neurofibrils are in the center of the rosettes. Such a clear-cut histologic picture, however, is not always seen. The less differentiated tumors are more embryonal and more malignant. The classification on a histologic basis of these tumors has tended to create confusion in the literature.

Neuroblastomas can occur wherever sympathetic nervous tissue is present but the usual site of origin of the primary tumor is in the abdomen. Farber² reviewed 40 neuroblastomas in children and found 32 having an intra-abdominal origin, four were retropleural, and four cervical. The tumor may arise in the medulla of the adrenal or in any of the ganglia extending from the cervical area to the pelvis. Neuroblastomas arising in the adrenal medulla have been adequately reviewed by Redman, *et al.*,³ while neurogenic tumors arising in the thorax have been discussed from the roentgenologic viewpoint by Kornblum and Bradshaw,⁴ and Wyatt and Farber.⁵ A dense, rounded shadow in the posterior portion of the chest is considered of diagnostic importance. The symptomatology of primary thoracic tumors is negligible until pressure of an enlarging tumor and evidence of metastasis become evident. The presence of an intrathoracic neuroblastoma in early infancy, without metastasis and without pressure symptoms, offers a difficult diagnostic problem, and this is especially true when the symptoms are not associated with pulmonary pathology. To overlook such a lesion is an unfortunate circumstance, as recourse to surgical intervention and roentgenotherapy (Ladd and Gross,¹ and Wyatt and Farber⁵) may give truly remarkable results.

We are reporting a case of a five-months-old infant who offered a puzzling symptomatology and who was finally diagnosed by aspiration biopsy under fluoroscopic guidance.



FIG. 1.—Liver margins as outlined by percussion.

Case Report.—Baby W. S., male, age five months, was referred, on June 18, 1941, to Dr. Gabriel Tucker at the Graduate Hospital, because of a radiopaque shadow in the lower lobe of the right lung. The baby had been apparently well until the age of three months, when he developed intermittent hyperpyrexia and began to perspire profusely, especially after feedings. On admission, the rectal temperature was 105.4° F. and later was 107.2° F. The infant was very restless and pallid. Respirations were shallow, accelerated, and dyspneic. The abdomen was markedly distended and the lower edge of the liver was below the transumbilical level (Fig. 1). There was marked suppression of breath sounds over the right lower lobe with flatness to percussion. It was felt that the child had an encapsulated process in the pleura or in the lung.

The child was given sulfathiazole, and the temperature declined by lysis. A total of 1643¾ grains of sulfathiazole was administered from June 18 to July 22.

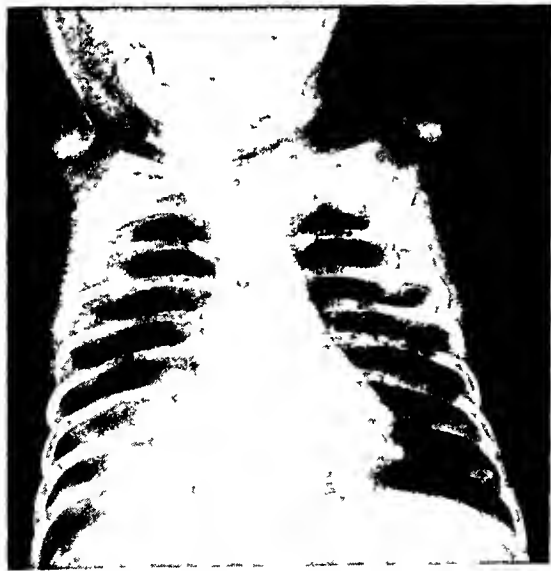


FIG. 2.—Radiogram taken preoperatively.



FIG. 3.—Radiogram taken preoperatively.

Roentgenologic examination, on June 18, showed: "In the examination of the chest, the bony thorax and cardiac silhouette and aorta are negative. The lung fields are also negative except for a sharply circumscribed, rounded, uniform density situated at the right base posteriorly, which is about 6 cm. in diameter. Both domes of the diaphragm move well, but the posterior mass moves very little with respiration, suggesting that it is attached to the posterior parietes. The swallowing function was negative, as tested by liquid barium. We suspect that the mass in the right lower chest is a loculated empyema." Subsequent roentgenograms (Figs. 2 and 3), on the 19th and 23rd of June, showed practically no change in the chest fields. At

INTRATHORACIC NEUROBLASTOMA

this examination, congenital lung cyst, solid lung tumor, and subdiaphragmatic tumor were considered.

One uranalysis revealed glycosuria and another a heavy trace of albumin. Urinary specific gravities ranged from 1.015 to 1.030. The white count on admission was 7,150, neutrophils 68%, basophils 2%, monocytes 2%, lymphocytes 28%. Red cell count on June 19 was 4,200,000, hemoglobin, 60% (10 grams); leukocytes 10,000, neutrophils 36%, monocytes 14%, lymphocytes 50%. The baby received a transfusion of 100 cc. of blood on June 19 and 120 cc. on June 20. On June 21 the red count was 5,620,000, hemoglobin 75% (12.5 grams); leukocytes 10,000; neutrophils 82%, monocytes 6%, and lymphocytes 12%. Agglutination tests were negative. Blood sugar on July 17 was 137 mg.



Fig. 4.—Urogram taken preoperatively.

When the abdominal distension was lessened by enemas, rectal tube and prostigmin the right kidney could be felt extending below the liver but it did not appear enlarged. A subcutaneous urogram (Fig. 4) on July 8 was reported as follows: "In the films made 10, 20 and 35 minutes after subcutaneous injection of diodrast, the left kidney pelvis was well visualized and appears normal. The left ureter is not seen. The right kidney pelvis is considerably smaller and is dislocated, possibly due to rotation of the kidney. The soft tissue outline of this kidney is not definitely identified but is visualized and appears slightly larger than one would expect with such a small renal pelvis. This suggests that the kidney may be filled by neoplastic cells. In several of the films, particularly that made at 45 minutes, there is a suggestion of a soft tissue mass at the superior pole of the right kidney, and this mass may be continuous with the previously described mass extending into the lower thorax. Although these findings are not visualized with sufficient clarity

to be conclusive, they, nevertheless, suggest the possibility of an adrenal tumor invading the right kidney and extending up into the lower thorax, either directly or by means of liver metastasis." A roentgenogram of the skull on July 10 revealed no evidence of metastasis. On July 15, roentgenograms of the long bones and bony thorax revealed no evidence of metastasis, and it was felt, at this time, that the mass in the chest had not increased in size.

Preoperatively, the infant had a very stormy course, accentuated by attacks of profuse perspiration, accompanied by accelerated breathing, restlessness, irritability and abdominal distension. On June 28 a biopsy specimen was obtained, under fluoroscopic guidance.

Pathologic Examination.—*Microscopic:* Dr. E. A. Case. "The sediment from this fluid consists mostly of blood, and the leukocytes are not numerous. Groups of cells occur, having a round, deeply stained nucleus larger than a lymphocyte and with little

or no cytoplasm. It is difficult to determine what these cells are but their appearance and arrangement suggest tumor cells but this is not certain. *Tentative Diagnosis:* Neurocytoma of the adrenal (Pepper type)."

Operation.—On July 23 it was felt that the child was in as good a condition as could possibly be hoped for, and an exploratory celiotomy was performed under ether anesthesia. The abdomen was opened in the upper right abdominal quadrant through an incision which passed along the outer edge of the right rectus muscle. The liver seemed to be perfectly normal, and upon displacing it a mass was found in the right spinal gutter. The kidney could be isolated and the adrenal could be seen very clearly. Both of these organs seemed to be normal. An opening was made through the posterior

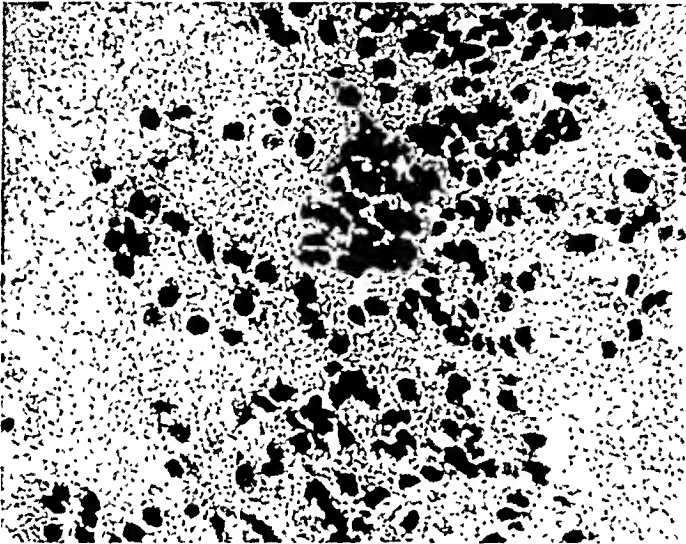


FIG. 5.—Photomicrograph of material aspirated from tumor.

parietal peritoneum and the mass which was uncovered was entirely separate from the liver. The liver was dislocated out of the abdominal cavity to the left, and it was found that the mass was not infra- but supradiaphragmatic, and it was necessary to incise the diaphragm and enter the right pleural cavity. The mass was found to be about the size of a small orange, and it corresponded to the shadow shown roentgenographically. The mass had a distinct capsule which made it possible to develop a line of cleavage and remove all of it except its hilum or pedicle, which was between two and three centimeters in width and attached to the bodies of the lower dorsal vertebrae. After clamping the pedicle, an incision was made across the tumor mass, which was then removed. This left some of the tumor behind with the pedicle. The pedicle was ligated by continuous suture ligature of No. 1 chromic catgut, and the opening in the diaphragm was closed with a continuous catgut suture, making it air-tight. The celiotomy wound was approximated by interrupted sutures of dermol. A transfusion was started during the operation. The infant was placed in an oxygen tent and, though his condition was fair at the close of the operation, he succumbed about three and one-half hours postoperatively.

An autopsy was performed, July 23, 1941, by Dr. Howard Lorenz, Resident Pathologist at the Graduate Hospital, and the pertinent facts from his report were as follows: *Thorax:* Upon opening the thorax it was first observed that the right chest cavity contained about 75 cc. of dark red blood. The right lung was fully collapsed. The left lung was well aerated. *Heart:* The pericardium was of average normal thickness, smooth and glistening. No adhesions or fluid were found in the pericardial sac. The heart weighed 55 Gm., was not enlarged, and the surface was smooth. There were no

INTRATHORACIC NEUROBLASTOMA

congenital lesions such as patent foramen ovale or persistent ductus arteriosus. The diaphragm revealed an incision measuring 6 cm. long, united with sutures. *Respiratory System*: The right lung—50 Gm. The left lung—50 Gm. The right lung was collapsed, dark blue mottled. The left lung was aerated and mottled with dark and light areas. No masses felt or seen. No mediastinal lymph nodes felt. *Sympathetic Chain*: A mass of tissue, yellow-brown, soft and papillary, was found along the right paravertebral (retropleural) ganglion chain below the 10th thoracic vertebra and attachment of the diaphragm.

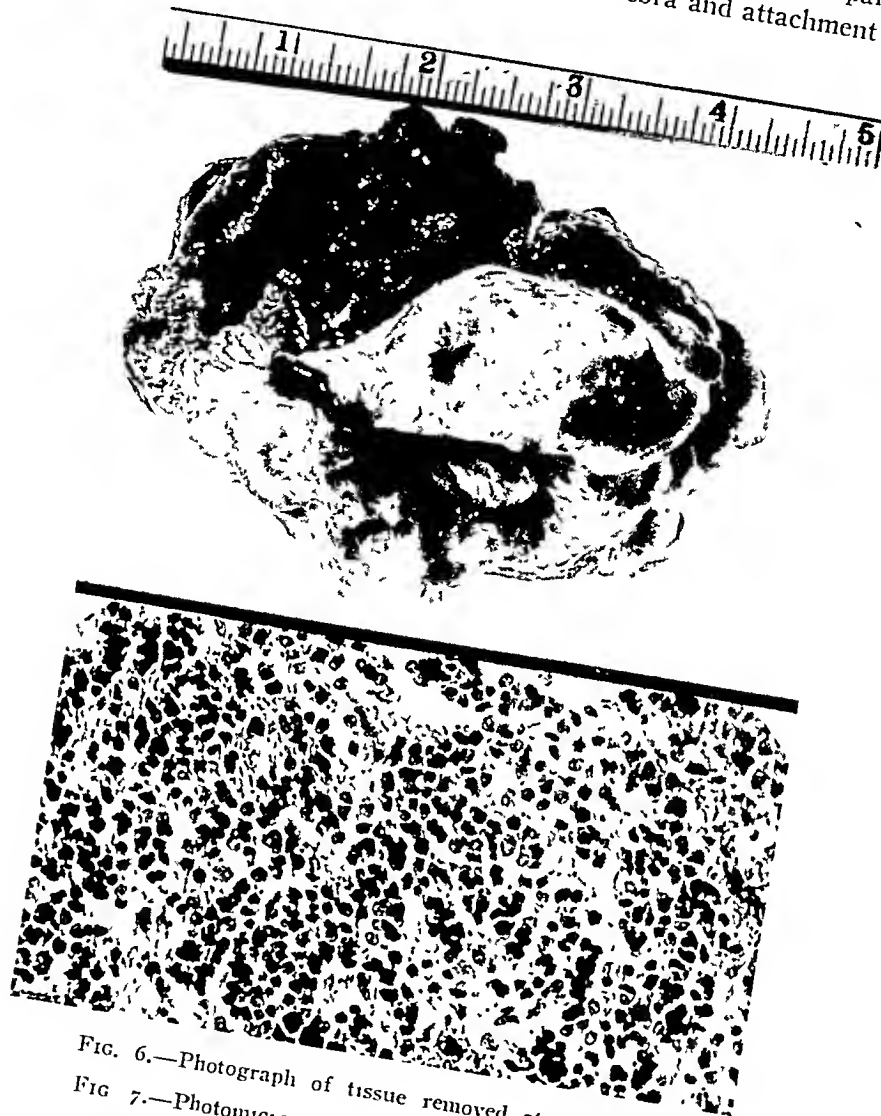


FIG. 6.—Photograph of tissue removed at operation.
FIG. 7.—Photomicrograph of section of tumor.

(This mass contained sutures). *Abdomen*: No ascites. *Gastro-intestinal Tract*: Gastro-intestinal tract was not explored in detail. *Liver*: The liver (400 Gm.) was somewhat enlarged with a smooth and homogeneous surface externally, and it cut easily. Cut surface appears homogeneous, with normal color except near the periphery in several areas, about 1 cm. wide and 0.5 cm. deep, where the color was a dark brown, almost black. Section of these areas were taken for microscopic examination. The gallbladder was bright green in color, soft, and no calculi were present. The pancreas was of moderate consistency and no masses were palpated. No evidence of necrosis was observed. The spleen weighed 25 Gm., and its capsule was wrinkled and dark. The cut surface was mottled with a sprinkling of white dots. The adrenal glands revealed no gross lesions. The right kidney (55 Gm.). Left kidney (38 Gm.) The cortex and medulla were normal in color. There was a small amount of peripelvic fat. *Gross Anatomic Diagnoses*:

1. Remains of tumor found along right paravertebral ganglion chain below 10th thoracic vertebra. 2. Collapsed right lung. 3. Right hemothorax. *Cause of Death:* Probably from hemothorax and associated shock.

Pathologic Examination.—Microscopic: Tumor. (Fig. 6) (Taken from sympathetic chain). The section (Fig. 7) shows several types of cells: (1) These have a large vesicular nucleus and very little cytoplasm, and resemble immature lymphoid cells. (2) Large eosinophilic cells with a large dark nucleus at the periphery. (3) Small lymphocytes. (4) Connective tissue cells with elongated nuclei and pink cytoplasm. (5) Here and there one sees cells which are as big as No. 2, and which stain similarly, but these have two nuclei, at the poles, with clear cytoplasm in between and in the center. In one case, it seems as if the cytoplasm had just broken in the center and two cells were formed. Rosettes are not seen. Ganglion cells are not seen. The specimen removed at operation was stained by the silver method. Many fibril-like strands are seen, which are probably connective tissue rather than nervous tissue. *Spleen:* Contains areas of hemorrhagic infiltration of pulp. *Lung:* (Right) Atelectatic. No definite evidence of metastatic tumor was found. *Adrenal Glands:* Normal. *Kidney:* Normal. *Sternum:* Shows no definite evidence of metastatic lesions. *Pathologic Diagnoses:* Tumor: Neurocytoma (atypical). Spleen: Hemorrhagic areas. Lung: Right—atelectasis; left—normal. Adrenals, kidneys, and sternum apparently normal.

SUMMARY.—Some of the cases reported have manifestations similar to those in adrenal chromaffinoma, which may be due to excessive adrenalin secretion or to "adrenergic" action, evidencing excitability, tachycardia, profuse perspiration, abdominal distension, vomiting and episodes of cardiac failure. These symptoms were quite noteworthy in this patient. Intrathoracic involvement may give either no definite physical signs or signs mimicking other types of thoracic pathology. Because of the location of the tumor in the posterior mediastinum, certain signs may arise from pressure on the lung, pleura, vertebrae, involvement of the spinal cord, and encroachment on the diaphragm and retrocardiac space. Metastatic lesions may be manifest by signs in distant regions of the body. Aspiration biopsy, under fluoroscopic guidance, would seem to be a logical procedure in some cases. In fact, it may even be beneficial, in that it may initiate hemorrhage and necrosis, with spontaneous resolution of the tumor. It has been reported that neuroblastomas may undergo hemorrhage, necrosis and spontaneous resolution, or differentiate into a benign ganglioneuroma (Ladd and Gross,¹ Cushing and Wolbach.⁶) Intrathoracic involvement may be mistaken for other types of pulmonary pathology, even with most painstaking roentgenologic studies. Once the diagnosis is definitely established, even in the presence of metastases, surgery and irradiation of the primary tumor and roentgenotherapy of the metastatic lesions is advisable. The remarkable experiences of Ladd and Gross,¹ and Wyatt and Farber^{2, 5} with neuroblastomas have shown that the prognosis is not hopeless even if only a part of the tumor is removed and distant metastatic lesions are present, if deep roentgenotherapy is administered.

CONCLUSIONS

Intrathoracic neuroblastoma, without metastases, and symptoms referable to the chest, offers a difficult diagnostic problem. Aspiration biopsy is

INTRATHORACIC NEUROBLASTOMA

a valuable adjunct to other diagnostic aides. Early recognition of these tumors and prompt treatment, both surgical and roentgenologic, will materially enhance the prognosis.

REFERENCES

- ¹ Ladd, William E., and Gross, Robert E.: *Abdominal Surgery of Infancy and Childhood*. W. B. Saunders Co., Phila., and London., 1941.
- ² Farber, S.: Neuroblastoma. Abstract in *Am. Jour. Dis. Child.*, 60, 759-751, September, 1940.
- ³ Redman, J. L., Agerty, H. A., Barthmaier, O. F., and Fisher, H. R.: Adrenal Neuroblastoma: Report of Case and Review of Literature. *Am. Jour. Dis. Child.*, 56, 1097-1112, November, 1938.
- ⁴ Kornblum, K., and Bradshaw, H. H.: Intrathoracic Neurogenic Tumors. *Radiology*, 37, 391-406, October, 1941.
- ⁵ Wyatt, G. M., and Farber, S.: Neuroblastoma Sympatheticum: Roentgenologic Appearances and Radiation Treatment. *Am. Jour. Roentgenol.*, 46, 485-495, October, 1941.
- ⁶ Cushing, H., and Wolbach, S. B.: The Transformation of a Malignant Paravertebral Sympathicoblastoma into a Benign Ganglioneuroma. *Am. Jour. Path.*, 3, 203-216, May, 1927.

EMPHYEMA COMPLICATED BY BRONCHO-ESOPHAGO- PLEURAL FISTULA

J. K. BERMAN, M.D.

AND

C. E. WALTERS, M.D.

INDIANAPOLIS, INDIANA

FROM THE DEPARTMENT OF SURGERY, INDIANA UNIVERSITY SCHOOL OF MEDICINE, AND THE SURGICAL SERVICE OF THE JAMES WHITCOMB RILEY HOSPITAL FOR CHILDREN, INDIANAPOLIS, INDIANA

PERFORATIONS OF THE ESOPHAGUS are not uncommon. They may be due to foreign bodies, strong chemicals, carcinoma, peptic ulcer, rupture of a diverticulum, trauma, or they may occur spontaneously during severe vomiting. Such perforations may cause a mediastinitis or empyema, or both.

Perforation of an empyema into the esophagus is a rare event. According to Blauvelt¹ rib resection in the treatment of empyema was first advised by Arbutnot Lane, in 1882. Since then, 13 cases of pleuro-esophageal fistula, with empyema, have been reported, nine cases by Blauvelt, one of which was his own. Kanter and Madoff² reported one case in addition to their own. Torbett and Bennett³ reported one case of their own and one by Fonte.⁴ Gott⁵ reviewed 40 cases in 1933, and added four cases of spontaneous rupture. Most of these fistulae originated within the esophagus.

Zuppinger⁶ reported a case of perforation of the esophagus and empyema wall by inflammation of a mediastinal lymph node due to tuberculosis. He reports similar cases by Korner, Volleker and Verlaie. The perforations were at the level of the bifurcation of the trachea and there was no associated empyema. He also mentions one case in a tuberculous child of a communication between the esophagus and trachea, which was discovered at autopsy. Three similar cases were described by Lebland, Polandt and Quincke according to this author. All were tuberculous and none had empyema. Of the 13 cases reviewed by Blauvelt, Torbett and Bennett, five died and eight recovered. In no case was closure effected surgically, although this is mentioned as a possibility by Blauvelt.

We have been unable to find a report of broncho-esophagopleural fistula either as a cause or result of empyema. The following is a report of such a case:

Case Report.—David A., white, male, age 23 months, was admitted to the James Whitcomb Riley Hospital October 6, 1941. His aunt stated that the child was desperately sick, and that everything he ate or drank drained to the outside through a tube in his chest. Also, the milk which was injected into the abdominal tube came out through the chest opening.

Past History.—The following summary is from information given by the child's aunt, and the family physician: The child was a full term baby, delivered without

BRONCHO-ESOPHAGOPLEURAL FISTULA

complications, who weighed seven pounds at birth. His father is 27 years old, and in good health. His mother is 22 years old, and is now pregnant. There are three other children. One sister is described as being "subnormal." The patient had been apparently in good health until his present illness, which began in July, 1941, when he was 20 months old. The exact time of onset is not known but the referring physician described the early symptoms as "listlessness, fever, loss of weight and appetite." These symptoms persisted for six weeks before a physician was consulted. At this time (August, 1941) chest roentgenograms and thoracentesis revealed a massive empyema from which thick, creamy pus was aspirated. Streptococci and smaller numbers of staphylococci were identified as the causative organisms. Cultures were not made. A portion of the seventh rib was resected in the posterior axillary line and about 300 cc. of pus was evacuated. On the fourth postoperative day all food and liquids taken by mouth appeared on the chest dressings. Roentgenograms, after a weak barium mixture given by mouth, revealed an "esophageal fistula evidently communicating with the empyema cavity." Since all feedings were being lost, a gastrostomy was performed. This functioned well only if the tube was inserted into the duodenum. The boy had lost ten pounds in three months. On admission, the patient was a pale, poorly nourished child, with a temperature of 100.4° F. His weight was 18 pounds, 12 ounces. There was a draining surgical wound in the right chest, and a gastrostomy tube was in place, as previously described.

Laboratory Data.—The urine was essentially normal except for pentosuria on four occasions. Throat cultures (10/6/41 and 11/15/41) were negative for diphtheria bacilli. Blood studies showed the Kline and Mazzini tests to be negative. Hemoglobin 12.5 Gm. on admission, and ranging from 0.5 to 15 Gm. on dismissal from the hospital; R. B. C. 3,500,000, ranging from 2,200,000 to 4,000,000. W. B. C. 11,500, of which 28% were bands, 23% adult polys, 42% lymphocytes, 6% large monocytes, and 1% eosinophils, ranging from 7,250 to 25,500. In addition, basket cells, smudge cells, toxic granules, and plasma cells were reported at various times. Blood sugar 80 mg. per 100 cc. Gastric washings and throat cultures for pneumococci were negative. Culture from the chest drainage (11/20/41) showed *B. coli*, *Staphylococcus aureus* and hemolytic streptococci. Roentgenologic examination on admission showed increased bronchovascular markings in both lungs, with pleural thickening and fibrosis in the right base. There was no evidence of fluid or active disease in the right chest.

Course and Treatment.—On 10/14/41 lipiodol was injected into the esophagus through a catheter. This revealed tenting of the right border of the esophagus at the level of the 6th interspace with esophagobronchial fistula. At this time all food and liquid swallowed or introduced through the gastrostomy tube drained through the thoracotomy wound. A radiopaque catheter was introduced through the pylorus into the duodenum under fluoroscopic guidance. This permitted fairly satisfactory feeding through the tube. However, the catheter was either pulled out by the child or its end regurgitated by the continual vomiting, and it had to be replaced frequently. An esophagoscopy was undertaken 10/30/41, but the fistula could not be demonstrated. The patient was in a critical condition, temperature ranged to 103.5° F. Repeated blood transfusions and intravenous injections of normal saline and glucose were given. On 12/8/41 the old thoracotomy wound was opened so that more adequate drainage could be secured. A large amount of pus was evacuated. There was some improvement following this procedure and the temperature returned to a lower level, ranging to 100° F. daily.

On February 16, 1942, iodized oil was introduced into the empyema cavity under fluoroscopic guidance. The oil was seen to communicate and to outline the bronchial

tree and esophagus (Fig. 1). This indicated a broncho-esophagopleural fistula. The fistula between the empyema cavity and esophagus was clearly seen. It formed a narrow sinus tract measuring about 2.5 cm. in length. The oil promptly entered from the distal esophagus into the cardia of the stomach. There was no evidence of cardiospasm or obstruction in the lower esophagus.

On February 24, 1942, operation was performed under ether anesthesia. An incision was made over the 8th rib. At a previous operation a portion of the 9th rib had been removed. The 8th and the remaining portion of the 9th rib were now excised. The pleura was greatly thickened. The empyema cavity was large and extended up to the 5th interspace. The child's condition was poor and it was decided to decorticate the cavity in two stages. Accordingly, the lower portion was unroofed and two lengths of one-inch Penrose drains were inserted. The skin was closed loosely about the drains. Following the operation 150 cc. of whole blood and 500 cc. of normal saline, with 5% glucose, were given intravenously. A moderately severe reaction occurred after the operation. The temperature rose to 102.5° F., and pulse to 140. By the fourth postoperative day the temperature had returned to its previous levels of 99°-100° F.



FIG. 1—Roentgenogram showing broncho-esophagopleural fistula. Iodized oil was injected through the thoracotomy wound (Retouched)



FIG. 2—Roentgenogram showing esophagus after a barium meal. The fistulae are closed, and all wounds have healed (Retouched)

Seventeen days later a transfusion of 75 cc of whole blood was given. The second stage of the operation was performed on the following day (March 13, 1942) under ether anesthesia. A transverse incision was made over the 6th rib and a bipedicle flap of skin was elevated and retracted downward. This was done so that it would cover the large wound after granulation tissue filled the empyema cavity. The flap remained viable and prevented extensive scarring. The 6th and 7th ribs were removed

BRONCHIO-ESOPHAGOPLEURAL FISTULA

and the remainder of the thickened parietal pleura excised, thereby, completely decor-ticating the empyema cavity. Our exposure was excellent, and the child's condition was much better than at the previous operation. The broncho-esophageal fistula was easily identified. The esophagus was dissected loose from the bronchus by blunt and sharp dissection and the fistula closed with interrupted No. 00 chromic catgut. The bronchus was dealt with in a similar manner. The cavity was packed with vaselized gauze.

Feedings were continued through the gastrostomy tube. On March 20, 1942, another transfusion of 150 cc. of whole blood was given, and feedings were started by mouth with no leakage. The gauze packing was removed on March 22, 1942, and lightly replaced. It was removed one week later. The child was eating voraciously, and the gastrostomy tube was removed. The bronchopleural fistula was now apparent again, although the cavity was filling in very rapidly.

On May 8, 1942, the patient contracted varicella and was transferred to the iso-lation ward. This did not retard his progress, and the chest wound had entirely healed by June 1, 1942. His condition was excellent. There was no increase in temperature, and his weight was 25 pounds.

There remained one more task. The gastric fistula though small was persistent and annoying. The skin of the abdomen was excoriated due to the digestive action of the gastric juice. Conservative measures were unavailing. Therefore, the fistula was excised on July 14, 1942. Recovery was uneventful. The meal a roentgenogram of the esophagus, after a barium meal, July 30, 1942, revealed a spike-like deformity on the lateral esophageal wall in its middle third. (Fig. 2). The meal no leakage, but a small amount of barium remained in the defect. The meal passed readily into the stomach. The patient was discharged August 6, 1942.

Pathology.—We have considered the various ways in which this rare complication might have occurred. The possibilities may be divided under two heads: (1) Perforation of the esophagus as a *cause* of the empyema and fistulae; (2) Perforation of the esophagus as a *result* of the empyema.

(1) A suppurating mediastinal lymph node may have produced a traction diverticulum due to dense adhesions and then caused a perforation of the esophagus and bronchus. Such a condition is possible. The esophagus is apparently pulled to the right and appears to have a traction diverticulum. This supposition implies that the perforation was the cause and not the result of the empyema. It is difficult to reconcile the three-way communica-tion by this method. An erosion connecting the esophagus and bronchus could occur, but it is difficult to explain the opening into the pleura in this manner. Because either fistula would provide an exit for the small area of suppuration delimiting further extension.

A congenital anomaly may have preceded the empyema. The trachea and esophagus are formed from the primitive foregut. Lateral grooves appear in 4-5 mm. embryos. These become deeper from below upward, finally separat-ing the anterior trachea from the posterior esophagus. The lung bud appears as a projection of the anterior wall of the foregut in 4 mm. embryos. Before the trachea bifurcates to form the primary bronchi there appears on its right side the tracheal bud of the upper lobe of the right lung. This bronchial

bud is developed only on the right side and appears in embryos of 8-9 mm. Various types of congenital tracheo-esophageal fistula may occur. Excellent reports of these anomalies have been reported by Lanman,⁷ Leven,⁸ and Carter.⁹ Our case may have had a thin membrane separating the esophagus from the right main stem bronchus which perforated following a pneumonia. Such a perforation would have to take place at the junction of these two structures in order for both to communicate into the pleural cavity. Although this would be a type of anomaly not previously reported, it would explain the large broncho-esophageal fistula. It would be similar to type 3c in Lanman's classification of anomalies, but would constitute a connection of the esophagus with the right main stem bronchus instead of the trachea.

(2) The child may have had a right-sided pneumonia followed by empyema. This, in turn, was complicated by inflammation of the esophagus, ulceration or necrosis and perforation. This concept does not explain the fistula into the right bronchus which communicated not only with the esophagus but with the pleural cavity as well. Furthermore, it is not likely that pus would burrow into the esophagus and then the bronchus and then connect the two. It is more in accordance with experience that, having found an outlet, as in empyema necessitatis, this would suffice especially after rib resection and open drainage.

The course of events may be as above described. The large tube introduced through the thoracotomy may have eroded through. Against this idea is the observation that the esophagus is pulled to the affected side. Since the mediastinum and its structures are very mobile in a child of this age, the esophagus would be pushed to the opposite side. Furthermore, it would have been necessary to exert continuous mesial pressure on the tube to produce this effect.

We are of the opinion that this rare group of complications is the result of at least two factors: First, some congenital anomaly of the esophagus and bronchus; and, second, an erosion through the anomalous area by the empyema.

CONCLUSION

A case of empyema complicated by broncho-esophagopleural fistula is described. It was successfully treated by stage-operations and surgical closure of the fistulae.

The author gratefully acknowledges the cooperation of Drs. Arthur P. Echternacht and John Campbell, of the X-ray Department, Indiana University Hospitals.

REFERENCES

- ¹ Blauvelt, Hugh: Pleuro-esophageal Fistula in Empyema. *Brit. J. of Surg.*, **26**, 46, 1938-39.
- ² Kanter, A. J. and Madoff, Irving: Esophagopleural Fistula in a Case of Tuberculous Pneumothorax. *Am. Review of Tuberculosis*, **35**, 190, 1937.

BRONCHO-ESOPHAGOPLEURAL FISTULA

- ³ Torbett, J. Walter, and Bennett, A. C.: Esophagopleural Fistula: A Complication of Empyema. *Am. J. of Surg.*, 52, 129, 1941.
- ⁴ Foute (Quoted by Kanter and Madoff): *Brazil Medico Reo* d Jan., 36, 2, 1922.
- ⁵ Gott, R., Jr.: Spontaneous Rupture of the Esophagus: With a Report of Four Cases. *Am. J. of Med. Sc.*, 186, 400, 1933.
- ⁶ Zuppinger, C.: Zur Kenntnis der nicht traumatischen Oesophagoperforationen im Kindesalter. *Jahrbuch f. Kinderheilkunde*, 67, 444, 1903.
- ⁷ Lanman, Thos. H.: Congenital Atresia of the Esophagus. *Arch. of Surg.*, 41, No. 5, 1060, 1940.
- ⁸ Leven, N. L.: Congenital Atresia of the Esophagus with Tracheo-esophageal Fistula. *J. Thoracic Surg.*, 10, 648, 1941.
- ⁹ Carter, B. Noland: An Operation for the Cure of Congenital Atresia of the Esophagus. *S. G. O.*, 73, 485.

SUBSTITUTION OF THE URINARY BLADDER WITH A SEGMENT OF SIGMOID

AN EXPERIMENTAL STUDY

J. DEWEY BISGARD, M.D.

OMAHA, NEBR.

TOTAL RESECTION of the urinary bladder necessitates the provision of some method of urinary disposal. Several methods have been proposed and utilized, but all are attended by certain objectionable features. The most satisfactory method and the one employed almost exclusively is that devised by Coffey.¹ In this operation the ureters are transplanted into the sigmoid and the urine evacuated with the stools. Because the ureters open into a field which is constantly teeming with pathogenic bacteria, ascending urinary tract infections develop subsequently in a large percentage of cases, and not infrequently these infections are ultimately fatal. There are also the objectionable features of more or less frequent evacuations of liquid stools and of the psychologic effect of the loss of the act of micturition.

On the assumption that it was both possible and feasible to substitute bladder function and to use an isolated segment of the sigmoid as a substitute bladder, a two-stage operation was planned and put to experimental trial. The operation has been carried through to completion in two of the three female dogs in which it was attempted.

The technic of the operation is outlined in the illustrations in Plate I. It was performed in two stages. At the first stage the right ureter was divided at its junction with the bladder and dissected from its bed sufficiently to allow its transplantation to a loop of the sigmoid which had been selected to replace the bladder. The most proximal portion of the sigmoid which could be carried down to the position of the bladder without tension was selected. The ureter was transplanted by means of a strangulation suture at the head of a 1.5 cm. submucosal bed, as described by Coffey in his revised aseptic technic.¹ Four or five centimeters above this point the sigmoid was divided between clamps with a cautery. The distal end was closed aseptically with two rows of sutures and dropped into the pelvis. The proximal end was brought out through the wound as a temporary colostomy. The abdominal wall was closed around the exteriorized proximal end, the clamp removed, and the free edge of the bowel sutured to the skin around its circumference. Within three or four days liquid stools were passed by rectum. On the 10th postoperative day, and for four days subsequently, the blind pouch of rectum and distal sigmoid was irrigated with salt solution until the solution returned clear.

On the 14th day the second stage was performed. This consisted of the following steps: The left ureter was divided at its junction with the

SIGMOID SEGMENT AS BLADDER SUBSTITUTE

bladder dissected from its bed and laid aside. The bladder was then resected and a small mushroom catheter threaded through the urethra from within out, with the mushroom-end remaining in the peritoneal cavity. The distal sigmoid was divided about three or four centimeters distal to the site of previous ureteral implantation. The mushroom-tip of the catheter was inserted into this isolated segment of sigmoid and secured within the lumen with a purse-string suture placed around it about one centimeter above the free edge. With traction applied to the catheter beyond the meatus by an assistant, the open end of the isolated pouch of sigmoid was drawn down to the cut end of the urethra and the two edges approximated with interrupted mattress sutures. The left ureter was then placed in a sub-mucosal bed and implanted directly into the lumen of the pouch. The colostomized, or proximal end of the sigmoid was dissected free from the abdominal wall and the continuity of the bowel was reestablished by an end-

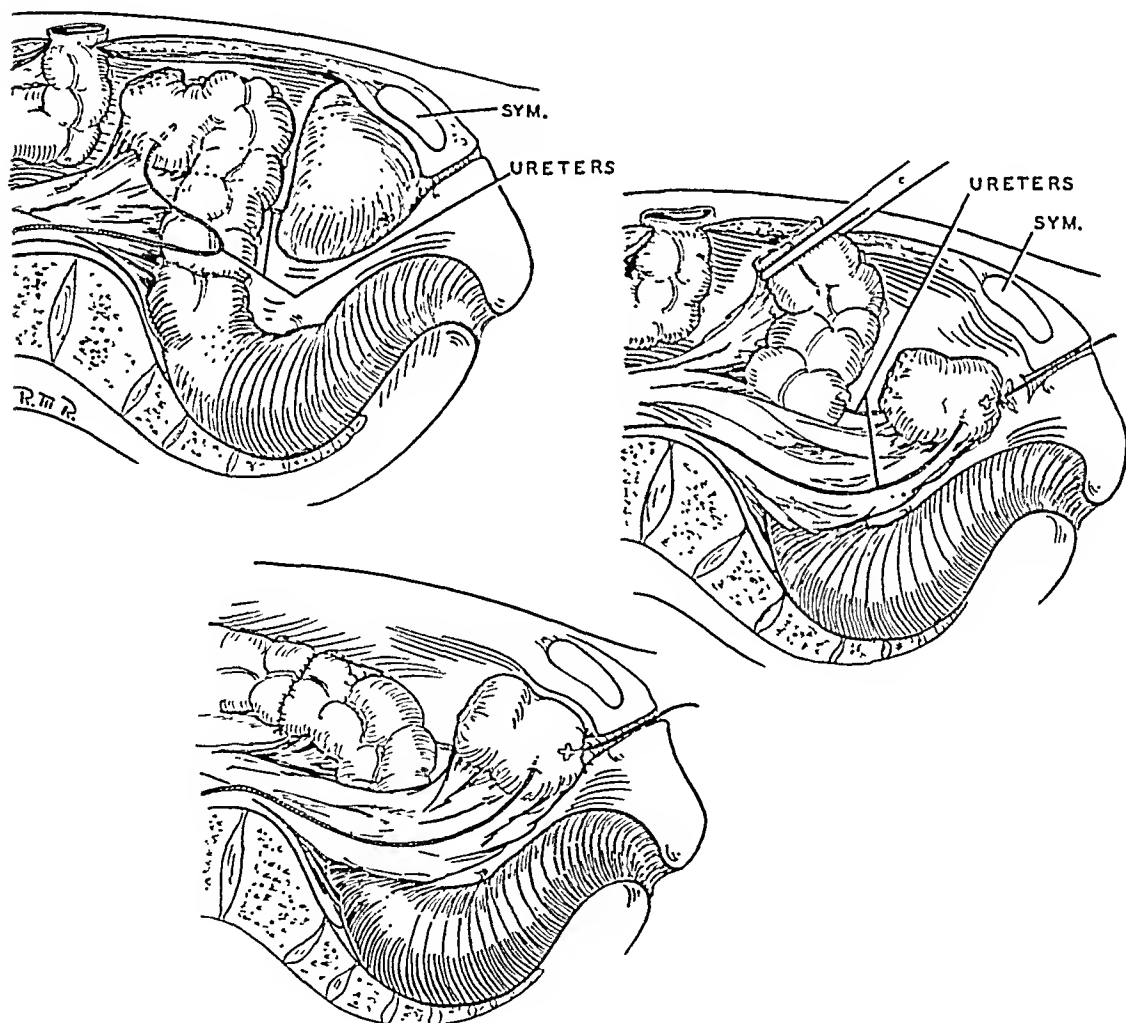


PLATE 1.—At the first stage (left) the right ureter is transplanted to the segment of the sigmoid which will subsequently be utilized as a substitute bladder. The bowel is divided above this point, the distal end infolded and the proximal end exteriorized as a colostomy.

The other two drawings show the steps of the second stage; the lower one the completed operation. These steps consist of resection of the bladder, transplantation of the left ureter, isolation of the sigmoid bladder, and suture of its distal free end to the urethra and reestablishment of continuity of the colon.

In man it would be safer to reestablish continuity of the colon by the Mikulicz's procedure. If, however, immediate direct anastomosis were performed as shown above, a vent should be provided by means of a proximal colostomy or cecostomy.

to-end anastomosis between it and the free end of the distal sigmoid. After closing the abdomen the catheter was cut off at the urethral meatus and fixed to the meatus with a suture. Five days later it was removed.

Both animals promptly developed urinary continence and, although the



FIG. 1.—Specimen from a dog sacrificed four months after completion of the second stage. Note normal appearance of the kidneys, ureters and sigmoid bladder. Also note well healed line of fusion between the sigmoid and urethra.

sigmoid pouch would retain an installation of at least four ounces for 15 minutes or longer, it emptied so efficiently that there was always less than one-half ounce of residual urine on several determinations. Within a month after operation the urine contained only an occasional pus cell, and if white cells are a measure of infection then there was no infection up to the time that the animals were sacrificed (three months later). Apparently perfectly well, they were killed merely to obtain the specimens.

Thus, four months after the second stage of the operation the kidneys and ureters were completely normal. There was no evidence of dilatation or inflammation of either the kidney pelves or ureters. The bladder pouch did not differ from normal sigmoid. Its mucosa showed no evidence of irritation or inflammation and no metaplastic change. Photographs of the gross specimen of one animal appear in Figure 1. Bacteriologic studies of the urine and studies of motor function of the pouch are now being made.

By dividing the operation into two stages, two important objectives were accomplished. Continuous urinary excretory function was assured. The success of the first ureteral transplant was established before disturbing the

SIGMOID SEGMENT AS BLADDER SUBSTITUTE

other ureter, thus avoiding the hazard of anuria. By diverting the fecal current through the temporary colostomy, and as a result of irrigations, the distal pouch was rendered relatively aseptic. This made it possible to isolate the segment of sigmoid and to carry through the rest of the operation with but slight risk of peritonitis.

CONCLUSIONS

A two-stage operation for resection of the urinary bladder and for its replacement with an isolated segment of sigmoid is presented. The operation has been performed successfully in two dogs; and by means of the sigmoid pouch normal urinary secretory and excretory functions were preserved, or rather reestablished. There was no evidence of an ascending urinary infection, but the period of observation was too short and the number of animals too few to evaluate the likelihood of this hazard.

There is no obvious reason for believing that this operation could not be utilized in man.

REFERENCES

- ¹ Coffey, R. C.: Production of Aseptic Uretero-enterostomy by a Suture Transfixing Ureteral Wall and the Intestinal Mucosa. *J. A. M. A.*, 94, 1748, 1930.
- Idem*: Transplantation of Ureters into Large Intestine by Submucous Implantation. *J. A. M. A.*, 99, 1320, October 15, 1932.
- Idem*: Further Studies and Experiences with Transfixion Suture Technic (Technic No. 3) for Transplantation of the Ureters into Large Intestine. *Northwest Med.*, 32, 31, January, 1933.

SO-CALLED RETROPERITONEAL LIPOMA

REPORT OF SEVEN CASES

J. SUTTON REGAN, M.D., S. SANES, M.D., AND JAMES D. MACCALLUM, M.D.
BUFFALO, N. Y.

FROM THE SURGICAL SERVICE—DR. JAMES C. SULLIVAN, ATTENDING—AND FROM THE PATHOLOGICAL LABORATORY—DR. KORNEL L. TERPLAN, DIRECTOR—OF THE BUFFALO GENERAL HOSPITAL, AND THE UNIVERSITY OF BUFFALO MEDICAL SCHOOL, BUFFALO, N. Y.

SO-CALLED RETROPERITONEAL LIPOMAS comprise a rather characteristic group of tumors. In addition to fatty tissue, these neoplasms may contain connective and mucoid tissue, bone, cartilage, and sarcomatous areas. Hence, some of them are properly referred to as retroperitoneal mixed mesenchymal tumors. The etiology of "retroperitoneal lipoma" is unknown. The most common site of origin is above the pelvis in the lumbar, perirenal, or pre-vertebral fat. Either side of the abdominal cavity may be involved. Occasionally the tumors are multiple or bilateral. They commonly give off large projections. Growth is generally slow but progressive. So-called retroperitoneal lipomas attain the largest dimensions of any solid abdominal tumor. They may extend from diaphragm to pelvis. They are lobulated, usually yellow in color, and encapsulated. Consistency varies, with soft, fluctuant, and firm areas. Regressive and inflammatory changes are prone to develop.

On the average, "retroperitoneal lipomas" are first recognized in patients between 40 and 60 years of age. Women are affected three times as frequently as men. Diagnosis of so-called retroperitoneal lipomas before operation or autopsy is difficult. Symptoms are few and obscure. They result from enlargement of the mass, its pressure on, and displacement of adjacent organs, regressive changes and malignant proliferation. In late stages "retroperitoneal lipoma" may produce emaciation, sometimes without definite loss of weight. Physical examination and radiographic investigation are of aid in localizing a tumor. The only possible treatment is operative. Removal of the tumor, however, may be hampered by its size and relation to neighboring structures. These factors help to explain the rather high incidence of operative mortality. Recurrence follows operation not only in tumors with sarcomatous areas but also in those diagnosed as histologically benign. For this reason "retroperitoneal lipoma," regardless of the microscopic picture, is considered by some authors as potentially malignant. The effects of radiation as a pre- and postoperative measure have not yet been definitely evaluated.

In the following seven cases, we record the surgical and pathologic experience with tumors in the group of "retroperitoneal lipoma and liposarcoma" at the Buffalo General Hospital, during the past ten years.

RETROPERITONEAL LIPOMA

CASE REPORTS

Case 1.—M. M., white, age 63, housewife, was admitted April 5, 1933. She died April 18, 1933. A hard lump had been noted in the lower right quadrant for three years. During the past year this lump had increased in size, with progressive enlargement of the abdomen. There was loss of weight of 16 lbs. Temperature 98–99° F.; blood pressure 160/90. Upon examination, the abdomen was enlarged, with a large, hard, nontender mass extending from costal margin to pelvis on right side. The ankles showed pitting edema.

Laboratory data.—Hemoglobin 60%; R.B.C. 3,490,000; W.B.C. 7600. Urine: Loaded with white blood cells and red blood cells.

Genito-urinary and radiographic examination: Chronic cystitis. Right catheter did not function. Upon being primed, it returned a small amount of cloudy, watery fluid with a trace of indigo carmine. Pyelogram of the right kidney showed it to be lying to the left of the spine in close proximity to the left kidney. *Clinical Impression:* Fibroid uterus.

Operation.—April 8, 1933: Avertin anesthesia. Long median incision. Enormous retroperitoneal tumor was present on the right side, extending from the ribs into pelvis, irregular in shape, more or less nodular; seemingly somewhat movable. The colon lay over the tumor, which also extended to the left side beyond the vertebrae. The upper pole of the tumor was in contact with the liver. Consistency was, for the most part, firm and hard; there were also cystic areas. The tumor could not be extirpated. Following operation the patient developed marked abdominal distention from paralytic ileus.

Postmortem findings: Retroperitoneal, lobulated, well encapsulated, lipomatous tumor, showing mucoid and edematous changes, necrosis, calcification, fibrosis, hemorrhages, and sarcomatous areas extending superiorly to right lobe of liver and inferiorly to brim of pelvis. Weight 18 pounds, measurements 33 x 20 x 10 cm.

Secondary effects of tumor: Concave depression in right lobe of liver; antero-medial displacement of colon, cecum and small intestine; dilatation of duodenum; compression of inferior vena cava, right iliac vein and artery; edema of legs; antero-medial displacement of right kidney to position opposite vertebral column, with compression atrophy of kidney; distortion of course of right ureter, with right hydro-nephrosis.

Other findings: Perforation of cecum; diffuse, fetid peritonitis; dilatation of small intestine; compression atelectasis of lungs; diverticulosis of colon; hypertrophic cirrhosis of liver, chronic splenic tumor; hemorrhoids; cholesterosis of gallbladder; hemorrhagic urethritis and cystitis; metropathia cystica, with small fibroid; aortic stenosis and insufficiency; hypertrophy of left ventricle.

Case 2.—C. W., white, male, age 83, was admitted November 6, 1935. He died November 21, 1935. The chief complaints were precordial pain radiating to both arms, and emesis for 1–3 days. Temperature 98–99° F.; blood pressure 110/50. Upon physical examination, the abdomen was distended with a large, nontender, immobile mass in right upper quadrant. Tympany was elicited in front of the mass. Bilateral indirect inguinal herniae were present.

Laboratory data: Hemoglobin 88%; R.B.C. 5,410,000; W.B.C. 14,000. Stools, positive test for occult blood. Urine: No remarkable data.

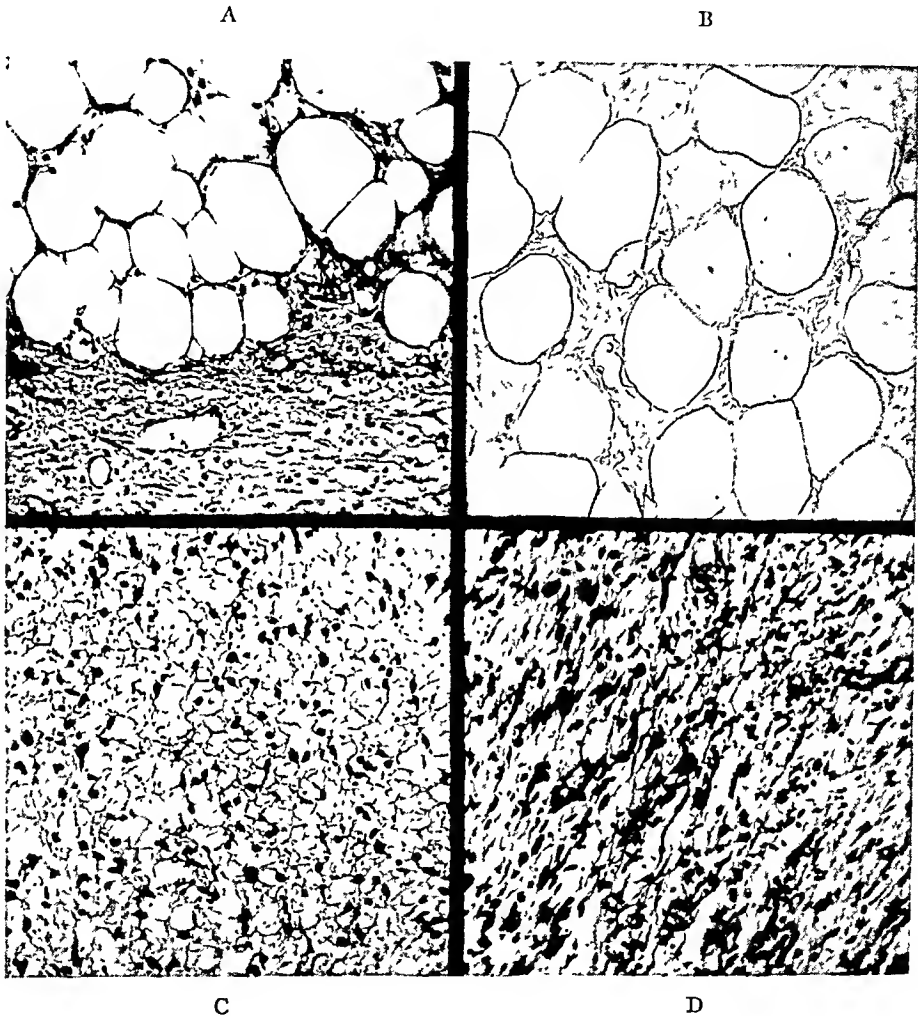
Radiographic examination: A plain film of the abdomen revealed increased density in the whole right upper quadrant. A gastro-intestinal series showed the stomach pushed to left side of abdomen, with constriction over lower portion above pylorus. There was a slight five-hour residue. The duodenum was pushed to left; its cap was irregular. An intravenous pyelogram showed the right renal pelvis at second lumbar vertebra. *Clinical Impression:* Retroperitoneal tumor.

Operation.—November 9, 1935: Avertin and novocain anesthesia. Abdominal

incision. Fatty, fibrous tumor, size of a grapefruit, was found, with origin in retroperitoneal space, firmly attached to transverse colon. Biopsy was taken. Postoperatively, patient developed mental, urinary, and respiratory symptoms.

Postmortem findings: Retroperitoneal, well encapsulated, soft lipomyxosarcoma (21 x 14 x 3 cm.) in front of right kidney firmly attached to second and third portions of duodenum, with purulent inflammation of anterior part of tumor in connection with an opening in lateral wall of third portion of duodenum.

PLATE I



A.—Fibrolipomatous structure, with hemorrhage and inflammation (Case 5).
 B.—Lipomatous structure, with regressive change (Case 1).
 C.—Edematous and myxomatous structure (Case 2).
 D.—Sarcomatous structure (Case 3).

Other findings: Coronary sclerosis with occlusion; myocardial infarction of left ventricle, with partial aneurysm and rupture; hemato-pericardium, chronic passive congestion of liver and spleen; marked lipomatosis of retroperitoneal, pelvic, pericardial and mesenteric tissue; hazelnut-sized lipoma of ascending colon; hypertrophy of prostate; hypertrophy of bladder, tracheobronchitis, fibrous, adhesive pleurisy; pulmonary emphysema.

Case 3.—V. L., white, female, age 53, was admitted August 9, 1935. She died August 14, 1935. For the past three years the abdomen had gradually increased in size. There was a loss of weight of 20 pounds. Five days before hospitalization pain

appeared in right lower quadrant. Temperature 98.6° F.: blood pressure 130/75. On physical examination, the abdomen was greatly distended. The distention was most marked in lower portion. Consistency of distended portion was soft. Percussion note over it was dull.

Laboratory data: Hemoglobin 80%, R.B.C. 4,400,000; W.B.C. 5,450. Urine: Several white blood cells. *Clinical Impression*: Ovarian cyst.

Operation.—August 10, 1935: Avertin, nitrous oxide-oxygen anesthesia. Right rectus incision. A solid, edematous tumor was found behind peritoneum on right side at level of ascending colon, extending to spleen. The tumor, which gave off about six tongue-like masses, was removed. During removal, duodenum was torn where tumor was adherent to wall of the second portion; the rent was sutured with chromic gut and linen. Terminal ileum, cecum, and colon were resected because the blood supply had been entirely removed from this portion of the intestine in excision of the tumor. The transverse colon was invaginated, purse-stringed with linen, and allowed to fall into the peritoneal cavity. Rubber tube was placed in the end of the small intestine and brought into wound. One large oilsilk pack and one large rubber tube drain were placed into tumor cavity. Transfusion. Postoperatively, patient developed fever, stupor, and respiratory symptoms.

Pathologic Examination.—*Gross*: Edematous, lipomatous tumor and five large masses composed of lobules. Surface of the tumor was smooth; color was yellow. Estimated weight 21 pounds; measurements 35 x 25 x 6 cm. Appendix, cecum, ascending colon, 24 cm. long. *Microscopic*: Lipofibromyxosarcoma, with edema and necrosis.

Case 4.—A. M., white, male, age 67, was admitted August 20, 1938. He died October 4, 1938. In 1935 a fatty tumor was removed from the "abdominal cavity" through a suprapubic incision; at the same time unilateral orchiectomy was performed. The abdomen had become enlarged for six weeks previous to present admission. There were swelling of the legs and dyspnea. The patient said that he was getting thin, but not losing weight. Temperature 98° F.: blood pressure 120/80. Upon examination, there was emaciation. The abdomen was markedly enlarged, tense, dull. The legs were edematous.

Laboratory data: Hemoglobin 92%, R.B.C. 4,050,000; W.B.C. 6,900. Urine: Occasional white blood cell. Gastric analysis: Free hydrochloric acid present.

Radiographic examination: A plain film of the abdomen was dense. A gastrointestinal series showed a filling defect at pyloric end of the stomach. It was narrow and irregular. There was a 24-hour residue. *Röntgenologic Diagnosis*: Growth of stomach. *Clinical Impression*: Retroperitoneal tumor (aneurysm?).

Operation.—August 22, 1938: Avertin-novocain anesthesia. Right rectus incision. A retroperitoneal, football-sized, smooth, dark mass attached posteriorly was palpated. No fluid was obtained on aspiration. No murmur was heard.

Postmortem findings: Retroperitoneal myxolipoma, with edema, hemorrhage, necrosis and inflammation on right side, apparently originating in right iliac fossa; weight 20 pounds, measurement 30 cm. in diameter. In addition there were several small retroperitoneal lipomas.

Secondary effects of tumor: Displacement of stomach, small intestine and ascending colon; thrombosis of iliac veins; edema of legs; slight hydrophrosis of right kidney.

Other findings: Aspiration of gastric contents in lungs, right adhesive pleurisy, brown atrophy of heart, diverticulosis of sigmoid, leukoplakia of esophagus.

Case 5.—O. W., white, female, age 41, was admitted to the hospital January 8, 1938. She was discharged, "recovered," April 28, 1938. Ten days before hospital entry the patient developed sudden, sharp pain in left side of abdomen, which radiated into left buttock and groin. She collapsed and was very restless. The pain required morphine for relief. Temperature 101° F.: blood pressure 120/70. Upon examination, a large mass occupied entire left side of abdomen, firm, not tender, not mobile on respiration.

Laboratory data: Hemoglobin 78%, R.B.C. 4,410,000; W.B.C., 18,200. Urine: Occasional red blood cells, white blood cells, and casts. Stool: Positive test for occult blood.

Genito-urinary and radiographic examination.—January 10, 1938: On left side, catheter passed to level of twelfth dorsal vertebra toward median line of spine. It flared outward and upward in this line. Pyelogram on left showed calyces not well visualized; right kidney showed concave irregularity in lower calix (cyst?). January 13, 1938: A large elliptical-shaped density on left side, occupied space between eleventh rib and crest of ileum, from spine to periphery of abdomen. Diodrast showed left kidney crowded upward. Right kidney was well demonstrated. *Clinical Impression:* Retroperitoneal tumor.

Operation.—January 15, 1938: Avertin-nitrous oxide anesthesia. A left "T" incision. Peritoneum was separated from parietal wall. A tumor, the left kidney, and a portion of the left adrenal gland were removed. Renal vessels were controlled with chromic gut ligature. Abdomen was closed with interrupted chromic gut and silkworm sutures. Penrose drain was brought out through left flank by stab wound.

Postoperative Course: Profuse drainage from wound developed. Subsequently incision healed except at drainage site. Roentgenograms revealed sinus leading to level of first and second lumbar vertebrae.

Pathologic Examination.—*Gross:* Large fatty tumor, 18.5 x 13.5 x 10 cm.; estimated weight seven pounds, surrounded by a distinctly distended capsule which contained injected veins and through which showed blood masses. Kidney was firmly adherent to capsule of upper part of tumor. On section, tumor exhibited a hemorrhagic pseudocyst within the subcapsular space, most pronounced at medial surface. The pseudocyst contained fluid and clotted blood. Most of the clots were adherent to wall, which revealed hemosiderosis. Renal pelvis was not distended. Ureter was cut 5 cm. below pelvis. *Microscopic:* Typical fibrolipoma, with hemorrhage, purulent inflammation and slight necrosis. Not malignant.

Case 6.—E. P., white female, age 47, was admitted April 27, 1941. She was discharged, "recovered," May 24, 1941. Twenty years previously the patient had had a pelvic operation. During the past five years a ventral hernia had developed in the incisional scar. Temperature 99.5° F.; blood pressure 150/90. Upon examination, an incisional, reducible hernia was found in a low suprapubic midline scar. Laboratory data: Urine: 25–30 white blood cells. *Clinical Impression:* Ventral incisional hernia.

Operation.—April 29, 1941: Nitrous oxide-oxygen-ether anesthesia. Incision to left of umbilicus, over hernia. In abdomen was found a huge retroperitoneal tumor which extended from liver on right side to costal margin on left side and to pelvis. Without difficulty the whole mass was brought out of the abdominal cavity. It was found to spring from right side of pelvis. With separation of peritoneum, the tumor was enucleated from its capsule. Excess peritoneum on right side, which had covered a portion of mass, was cut away. Peritoneum was freed on each side of incision and sutured; fascia was sutured. Skin was closed with silkworm and retaining sutures of dermal.

Postoperative Course.—There was a slight amount of fetid, purulent drainage from wound. On May 13, 1941, the wound was healed.

Pathologic Examination.—*Gross:* Encapsulated, lipomatous tumor, with marked edema and pseudocyst formation, measurements 39 x 30 x 8 cm.; weight 16.5 pounds. *Microscopic:* Fibrolipoma, with marked edema. No recognizable evidence of malignant change.

Case 7.—R. F., white, female, age 53, was admitted December 12, 1941. She was discharged "recovered" December 29, 1941. Four years previously the patient had an hysterectomy for fibroids. One month before admission an incidental examination disclosed a mass in lower abdomen. Temperature 98.6° F.; blood pressure 200/110.

Upon examination, an orange-sized, fixed mass was palpated in right lower quadrant arising from false pelvis.

Laboratory data: R.B.C. 4,900,000; W.B.C. 11,000, with 84% neutrophils, 1% eosinophils, 9% lymphocytes and 6% monocytes. *Clinical Impression*: Ovarian cyst.

Operation.—December 14, 1941: Nitrous oxide-oxygen-ether anesthesia. Low midline incision extending up beyond the umbilicus on the right side. Masses were felt behind the peritoneum, extending from the pelvic cavity to the right kidney. Multiple lipomas were removed. They had no connection with the kidney. Right ureter was seen behind the tumors. Sulfanilamide was dusted into the retroperitoneal spaces. Opening in posterior wall was closed with plain catgut. Chromic gut was used for muscle and fascia. No drainage. Postoperative course was uneventful.

Pathologic Examination.—*Gross*: Lipoma consisting of several ball-shaped tumors, varying in size from 8–13 cm. in diameter. Also, conglomerated orange- and grape-fruit-sized tumors connected with each other by fibrous tissue membranes. Weight of entire specimen 2,625 grams (one ovary also received). *Microscopic*: Fibrolipoma, with considerable number of atypical small giant cells and few multinucleated giant cells.

SUMMARY

The findings in our series of so-called retroperitoneal lipoma can be briefly summarized:

Age Incidence: In our seven patients the ages ranged from 41–83 years. Two patients fell into the fifth decade; two, into the sixth decade; two, into the seventh decade; and one, into the ninth decade. The average age was 58 years.

Sex Incidence: There were five females and two male.

Pathologic Findings: All the tumors were situated in the retroperitoneal tissue above the pelvis. In two cases, however, the tumor was thought to have originated in the pelvic cavity. The right side of the abdomen was involved six times. Five tumors were of the single type. In two patients, the lesion was multiple. Projections were given off from the main mass in two cases. The tumors were usually demarcated from surrounding tissue, lobulated, yellow to yellow-grey in color, and of varied consistency. Edema, pseudocyst formation, myxomatous changes, inflammation, and hemorrhage were frequent. The average weight was about 15 pounds. The largest tumor extended from diaphragm to pelvis. Tumors produced compression and displacement of liver, colon, duodenum, stomach, kidney, ureter, and inferior vena cava. Frank sarcomatous lesions were present in three cases. In two of these, which came to necropsy, metastases were not found.

Symptoms: Four patients complained of symptoms directly referable to the retroperitoneal tumor. Presence of a mass and gradual progressive enlargement of the abdomen over the period of three years was the most common complaint. In one patient, sharp pain, apparently due to subcapsular hemorrhage in the lipoma, brought the patient to a physician.

Three patients were not aware of the presence of the retroperitoneal tumor, until discovery of the lesion by a physician, who was consulted for (1) coronary occlusion; (2) incisional hernia; and (3) hypertension. Symptoms, on the basis of compression of adjacent organs by the tumor, included edema of legs, dyspnea, and vomiting. History of loss of weight

was elicited in two cases. One patient called attention to emaciation, without actual loss of weight.

Previous Operations: Three patients had celiotomies from 4-20 years before the last operation at the Buffalo General Hospital. In two of these patients the tumor had not been present at exploratory celiotomy 4 and 20 years previously; in one, a "fatty tumor" had been removed at the first operation.

Physical Examination: Five patients showed enlargement of the abdomen. Four times, a definite mass, which was not tender and did not move on respiration was palpated. Percussion note over the mass was dull or tympanitic. In two patients, with enlargement of abdomen and mass, outlines of the mass were not delineated.

Radiographic Examination: Roentgenologic studies were made in four patients. Pyelograms revealed displacement of kidney and ureter in two cases. In the other two cases, gastro-intestinal study disclosed displacement and obstruction of stomach and duodenum.

Clinical Impression: The diagnosis of "retroperitoneal lipoma" was not made preoperatively in any instance. Retroperitoneal tumor was the clinical impression in three patients; incisional hernia, in one, ovarian cyst in two, and fibroid uterus, in one.

Operative Reports: Six patients were operated upon *via* the transperitoneal route. The tumor could be removed in four cases. In one of these, along with the tumor, the cecum, ascending colon, and appendix had to be excised because of injury to blood supply; in another case, the kidney and portion of the adrenal had to be extirpated together with the retroperitoneal tumor. Factors which apparently influenced the operability of a tumor were size, encapsulation, and absence of incorporation with vital organs. Tumors removed, weighed 21, 7, 16.5, and 6 pounds respectively.

Mortality: Of the four patients in whom the tumor was extirpated, three recovered. Two developed drainage from the wound. The fourth patient of this group died three days after operation (excision of cecum, ascending colon, and appendix, suturing of duodenum) with fever, stupor, and respiratory symptoms. Three patients who had had celiotomies performed, but without removal of the retroperitoneal tumor, died 10-13 days following operation. The primary causes of death at autopsy were (1) peritonitis, from perforation of cecum; (2) rupture of heart from myocardial infarct, and peritoneal abscess in connection with sinus into duodenum, and (3) pulmonary aspiration of gastric content.

Irradiation: No patient received pre- or postoperative radiation.

REFERENCES

REPORTS ON "RETROPERITONEAL LIPOMA" IN THE AMERICAN LITERATURE DURING THE PAST 10 YEARS

Kretschmer, H.: Retroperitoneal Lipofibrosarcoma in a Child. Jour. Urol., 43, 61-74, January, 1940. (One case, with summary of literature)

- Blue, J. H., and Lafferty, C. R.: Perirenal Lipoma Surgery. 6, 944-946, December, 1939. (One case)
- Chown, B., Extraperitoneal Lipoma in a Child. Am. Jour. Dis. Child., 57, 401-403, February, 1939. (One case)
- Livermore, G. R.: Retroperitoneal Tumor Displacing Left Kidney. Jour. Am. Assn. Genito-urinary Surgeons, 31, 29-36, 1938. (One case)
- Ockuly, E. A., and Douglass, F. M.: Retroperitoneal Perirenal Lipomata. Jour. Urol., 37, 619-630, May, 1937. (Two cases, with summary of literature)
- Tolson, H. L.: Perirenal Lipoma. Urol. and Cutan. Rev., 40, 858-861, December, 1936. (One case)
- Harrington, S. W.: Retroperitoneal Fibromyxolipoma. Surg. Clin. N. Amer., 14, 636-638, June, 1934. (One case)
- Pemberton, J. DeJ., and Whitlock, M. E.: Large Retroperitoneal Lipoma. Surg. Clin. N. Amer., 14, 601-606, June, 1934. (One case, with review of thirty operated cases)
- Pemberton, J. DeJ., and McCaughan, J. M.: Intrarenal and Perirenal Lipomata. Surg. Gynec. and Obst., 56, 110-115, January, 1933. (Forty personal cases)
- Wechsler, L.: Retroperitoneal Perirenal Lipoma. New England Jour. Med., 206, 1259-1261, June, 1932. (One case)
- Bettman, R. B., and Serby, J.: Retroperitoneal Lipoma. Arch. Surg., 24, 300-307, February, 1932. (One case)

THE SURGICAL TREATMENT OF THE CONGENITAL MALFORMATIONS IMPLICATING THE DISTAL SPINAL CORD

JEFFERSON BROWDER, M.D.

BROOKLYN, N. Y.

FROM THE SURGICAL DEPARTMENT OF THE LONG ISLAND COLLEGE OF MEDICINE, THE NEUROLOGICAL UNIT OF THE BROOKLYN HOSPITAL, AND THE NEUROSURGICAL SERVICE OF THE KINGS COUNTY HOSPITAL, BROOKLYN, N. Y.

CONGENITAL ANOMALIES of the lumbosacral region comprise a variety of defects ranging from the innocent cleft of a single vertebral arch to the large meningocele with absence of fusion of the neural folds and with neither mesodermal nor ectodermal covering. Some patients with such malformations come under observation because of disturbances in function of the anorectal and vesicular sphincters and/or deformities of the lower extremities, the external evidence of an underlying defect in the nervous system having passed unnoticed or being absent entirely. Others are born with an obvious mass in the lower part of the back. Since the now classical description by von Recklinghausen¹ of a case of congenital clubfoot with hypertrichosis and spina bifida occulta, a number of excellent discourses have been recorded in the literature concerning the anatomicopathologic features of these anomalies,^{2, 3, 4, 5, 6} the concomitant disturbances in function of the extremities, and the alterations in neural mechanism of the vesicular and anorectal sphincters.^{7, 8, 9} Many methods of therapy have been advocated for the alleviation or cure of distressing symptoms that result from the maldevelopment.^{10, 11, 12, 13, 14, 15} There still remain, however, certain aspects of the therapeutic problem that have eluded satisfactory solution; consequently, many patients handicapped by lack of normal control of the urine and feces are unable to obtain desirable employment or to engage in social activities. Some of these can be rehabilitated by judicious surgery and it is with special reference to this method of treatment that the present paper is primarily concerned.

ANATOMIC AND PATHOLOGIC CONSIDERATIONS

It seems unnecessary at this time to review the recorded theories concerning the causative factors in the formation of congenital anomalies of the distal end of the spinal cord. Suffice it to say that a disturbance in the closure of the medullary folds in the embryo is quite generally held to be responsible for the maldevelopments. Normally, the neural folds in the cephalic and caudal regions are the last to close and, interestingly enough, the congenital anomalies are most commonly found in these areas. Examples are observed in which a failure in fusion of the vertebral arch or arches is the only telltale evidence that embryonal development did not travel at a normal pace. These are usually the cases of spina bifida disclosed by roentgenologic

ANOMALIES OF LUMBOSACRAL REGION

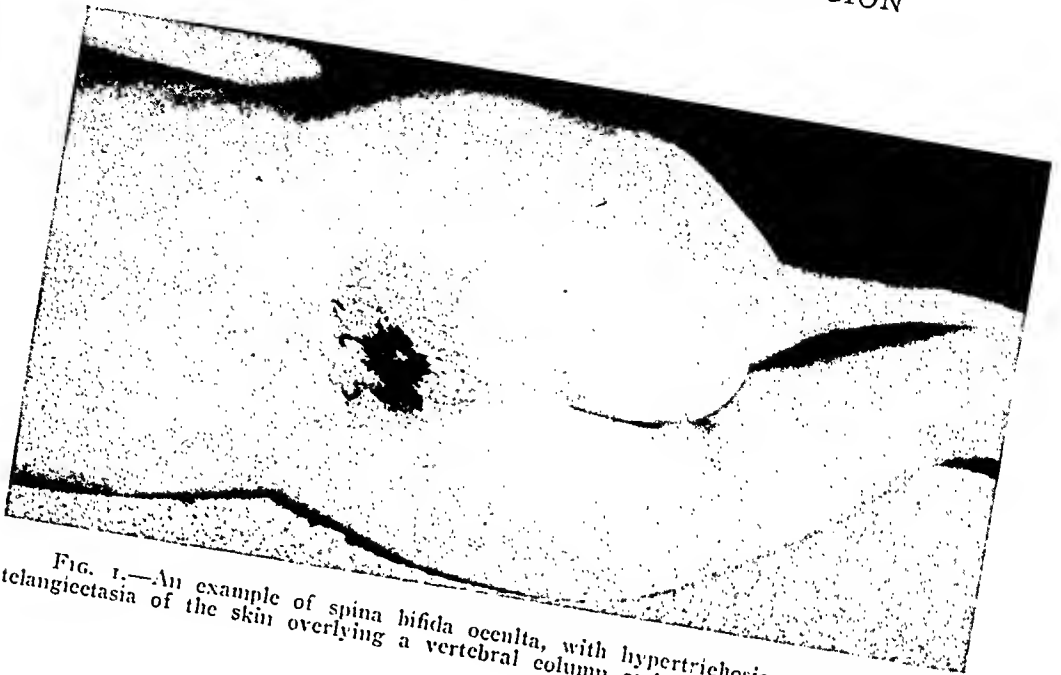


FIG. 1.—An example of spina bifida occulta, with hypertrichosis, and an area of telangiectasia of the skin overlying a vertebral column and spinal cord malformation.

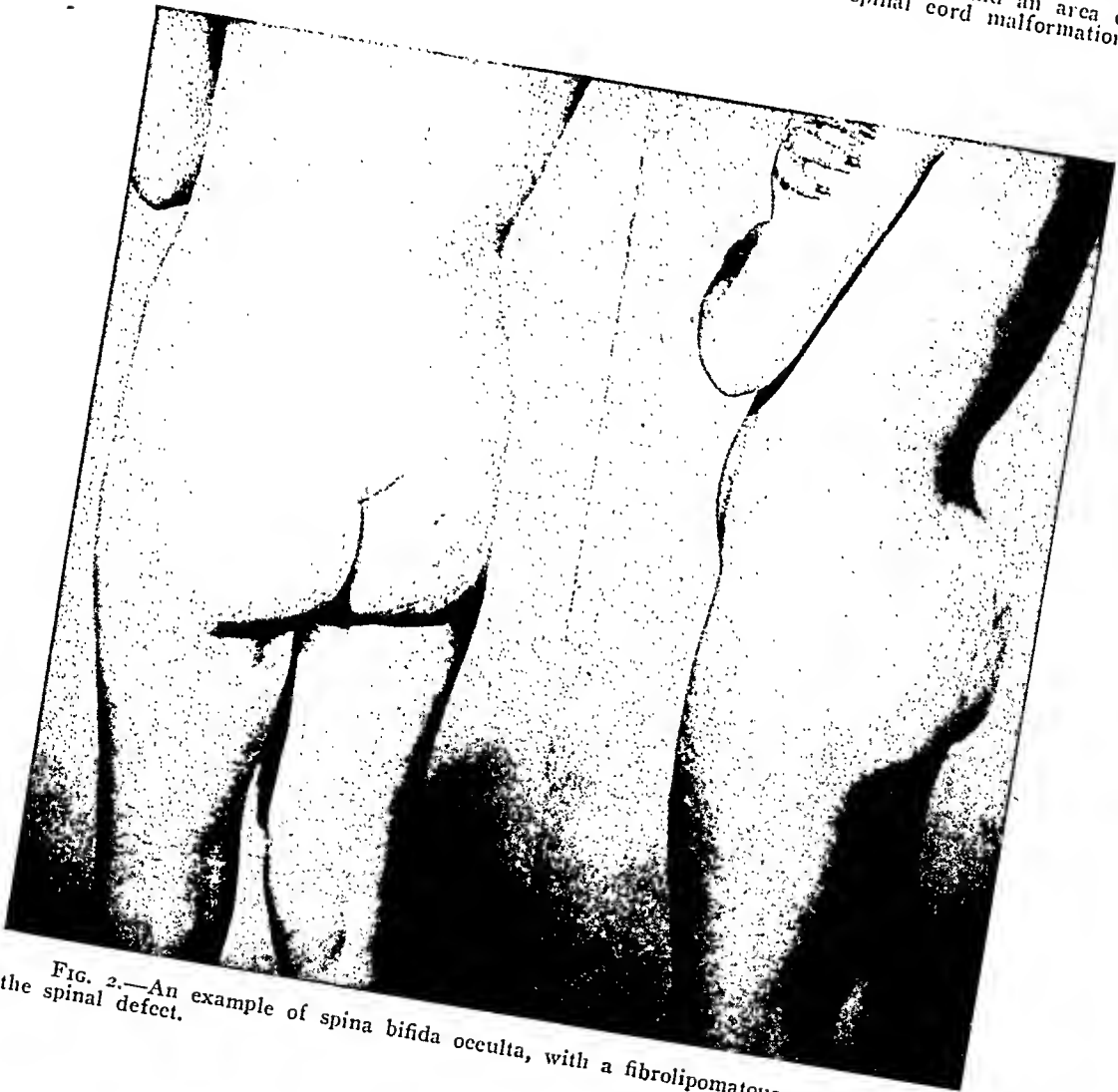


FIG. 2.—An example of spina bifida occulta, with a fibrolipomatous mass overlying the spinal defect.

examination. The presence of a dimple, a nipple, striae, telangiectasis, hypertrichosis or excessive pigmentation of the skin overlying any part of the cerebrospinal axis (Fig. 1) suggests an underlying defect. In some, there are symptoms and physical signs indicative of an accompanying disturbance referable to the nerve tissue. In others, without neurogenic dysfunction, maldevelopment of the mesoblastic elements is a prominent feature.⁶ This concept is readily comprehensible, for examples are seen that show extensive overgrowth of bone about the defective area without clinical evidence that the spinal cord or cauda equina is implicated. A most remarkable instance of this type came under my observation some years ago. In this patient two

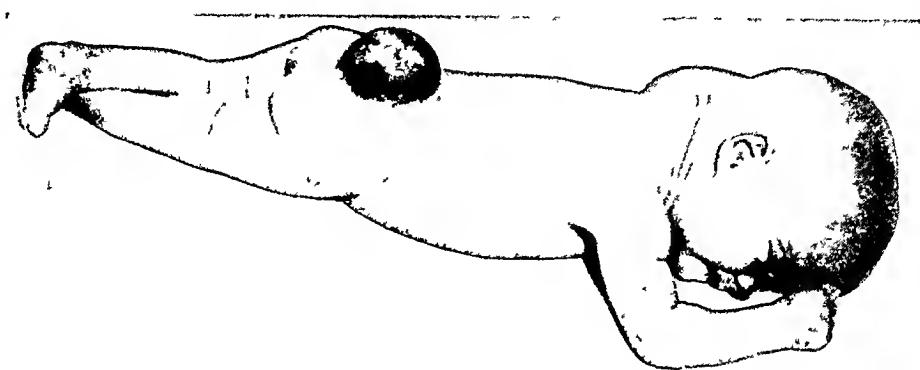


FIG. 3.—A meningocele of the lumbosacral area, with the spinal cord adherent to the dome of the cyst, as illustrated in Figure 4.

parallel sheets of bone, half the width of one's palm, lying deep in the subcutaneous tissue and extending from the sacrum to the occiput, were demonstrated roentgenologically. In the cervicodorsal region there was a joint-like mechanism that permitted limited flexion and extension of the head. The child was appropriately called by the house staff, the "armadillo-kid." Often imperfections of laminae in the lumbosacral area are accompanied by adherence of the dura to the overlying tissues but without evidence of implication of the intradural structures. In others a fibrolipomatous mass may occupy the epidural space at the site of the anomaly and this mass is connected by a fibrous stalk with a large fat pad situated subcutaneously (Fig 2). Occasionally the fatty mass extends into the dural envelope and is dispersed about the spinal cord or a large filum terminale and the adjacent spinal roots. A small dorsal protrusion of the meninges may be enclosed in the fibrolipoma and this trapped within the vertebral canal.¹⁵ If a meningocele is present, the vertebral arch or arches are widely defective and the cystic mass is covered with granulation tissue, with a parchment-like membrane, or with well-formed skin. The fluid-containing cavity in the mass may communicate freely with the subarachnoid space, or a portion of the meningocele may be composed of a compartment containing yellow fluid and not communicating with the subarachnoid space. In one instance in my experience, the mass comprised four separate cysts somewhat radially arranged about an obliterated lumen in the neck of a meningocele. Prolapse of a part of the cauda equina

ANOMALIES OF LUMBOSACRAL REGION

into the cavity of a meningocele may be the only abnormality of the nervous system demonstrable.¹⁶

The most common types of congenital malformation of the lumbosacral area are the meningomyelocele and the syringomyelocele frequently associated with defective developments in other parts of the neural tube, hydrocephalus being the most common. The exact relationship between these two conditions is not clearly understood. Patients with a malformation of the meningomyelocele variety usually present clinical evidence that the sacral portion of the spinal cord is functionless. This is readily understood when consideration is given to the

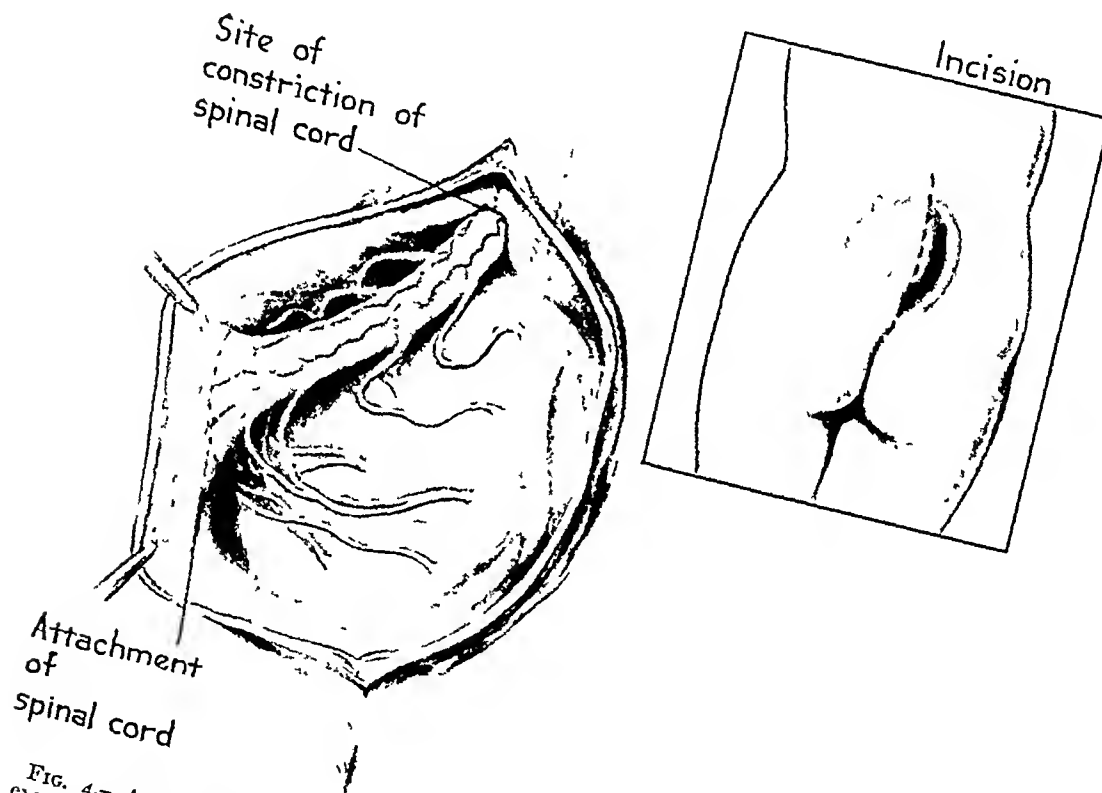


FIG. 4.—An illustration of an average example of a lumbosacral meningomyelocele as exposed at operation. The incision should be made to one side of the midline to prevent injury of the spinal cord.

gross alterations in development that are observed. In such examples, when the sac is opened at operation, there is frequently disclosed an abnormal appearing spinal cord terminating at the apex of the cavity and adherent along the dorsal cephalad portion of the cyst wall (Fig. 4). This termination of the cord is usually a somewhat fanned-out enlargement and several maldeveloped nerve radicals emerge from the mass. Distal to this there may be demonstrable a flattened-out, atrophic structure representing a part of the coccygeal portion of the neural tube, or in some instances a part of the sacral spinal cord as well. Other variations may be observed. The

deformed spinal cord may be cystic and, if opened, a communication with an enlarged central canal is visible. Infrequently the entire meningocele is lined with the thinned-out anomalous spinal cord, the nerve roots being demonstrated only after the neural tissue has been dissected from the dura.

Microscopic examination of the spinal cord immediately cephalad to the malformation usually discloses paucity of neural cells in the grey columns, variable degrees of dilatation of the central canal, and compression of both long and short fiber tracts (Fig. 5). At the site of attachment of the cord to the sac, changes are frequently so marked as to constitute a complete transverse lesion of the cord at this level. Segments of the cord distal to its attachment to the sac show imperfect development, in fact, the neural tissue is frequently scanty and fused with mesoblastic elements.

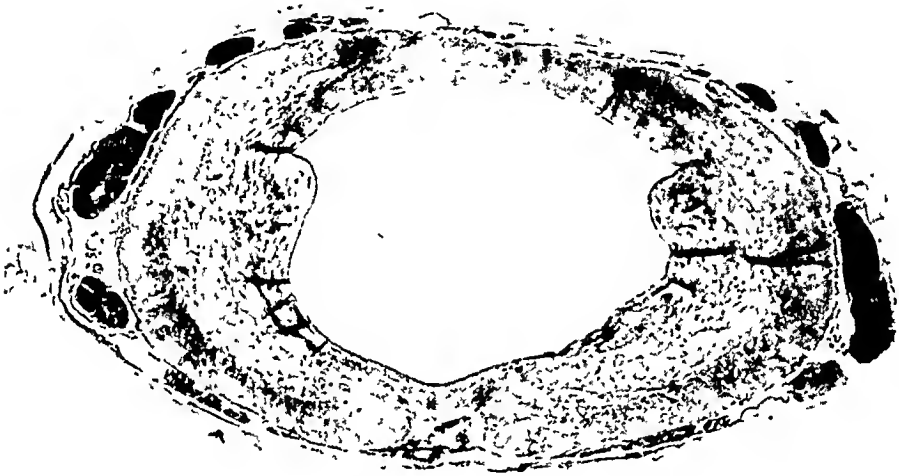


FIG. 5.—A section of the spinal cord just cephalad to a meningocele showing compression of both grey and white columns by the hydromyelia.

PHYSIOLOGIC FEATURES

The anatomic findings indicate that several features are to be given consideration in attempting to estimate the underlying reasons for functional disturbances observed clinically. One may comprehend, for the most part, at least those dependent upon gross defective development in the spinal cord. These consist, in the main, of alteration in function of the anorectal and vesicular sphincters, loss of cutaneous sensibility of the saddle area, and paresis to paralysis of the legs and feet associated with deformities of the feet and toes. Motor and sensory implication of the lower extremities depends upon the degree of neural involvement. It is to be remembered, however, that abnormal physical findings of neurogenic origin may change as the patient grows older. It has been observed in some infants with lumbosacral meningocele, that for several weeks after birth the urine is passed in quantities at intervals, the diaper remaining dry in the interim. As the meningocele increases in size dribbling of urine is observed, usually an overflow incontinence, however in some cases the sphincters eventually become relaxed and total incontinence ensues.

ANOMALIES OF LUMBOSACRAL REGION

In the normal embryo of three months the spinal cord extends the full length of the vertebral canal, but at about this time the "upward migration" of the cord begins, and at birth its distal tip has come to lie at the level of the third lumbar vertebra. The length of the vertebral canal continues to increase until full growth has been attained, without a comparable increase in the length of the spinal cord. Consequently, in adult life a normal spinal cord terminates at the lower level of the first lumbar vertebra. It seems well established that in most meningocele of the lumbosacral region, the spinal cord terminates in the dome of the sac. In many instances of so-called spina bifida occulta the defect in the vertebral arches, with a migration of the distal portion of the cord is so firmly anchored that upward conditions the distal portion of the cord is so firmly anchored that upward migration does not occur. At best, there may be only slight ascent, with a reduction in size of the lumbar and sacral spinal cord to about one-half the size of the thoracic cord (giant filum terminale). The inability for the spinal cord to ascend as the vertebral canal elongates places the cord on stretch and no doubt interferes with its normal development and possibly its intrinsic blood supply. Further traction may be placed on the cord if there is a slow progressive enlargement of the sac of a meningocele. Such abnormal tension is well illustrated by the Arnold-Chiari syndrome.¹⁷ In this condition the spinal cord is fixed at a point of defective development, and as the vertebral canal increases in length the structures within the posterior cranial fossa are partly drawn through the foramen magnum into the upper cervical canal. The degree of stretching produced by a fixation of the spinal cord in the lumbosacral region is probably even greater than that observed in thoracic or cervical malformations. In all events it seems reasonable to assume that this traction can produce additional disturbances as was described under the anatomic considerations may by virtue of its size press upon the neural structures thereby producing dysfunctions of the bladder, rectum and lower extremities.

While the neurogenic changes under consideration may be caused by gross defective development of the spinal cord, traction on a maldeveloped spinal cord and/or mesoblastic malformation within the vertebral canal pressing on the neural structures, examples have been encountered in which none of these appeared to play an important part. The following is a case in point:

Case 1.—A male, age 67, had enjoyed good health with the exception of an occasional acute respiratory infection. Since birth there had been a lump over the lower part of the back. He denied any disturbance of urination or sexual function prior to onset of the present illness. About one year before admission to the hospital there was noted slight difficulty of urination. This disturbance became progressively worse and three months before entry he resorted to the use of a catheter. A genitourinary specialist was consulted who failed to find hypertrophy of the prostate gland or other causes of urethral obstruction. The examination disclosed no abnormalities except those related to a congenital anomaly of the lumbosacral region. There was a

rounded, soft prominence over the distal part of the spine covered with well developed skin. The third, fourth and fifth sacral dermatome zones were anaesthetic and analgesic. The external anal sphincter was relaxed. The ankle jerks were absent bilaterally. At operation, the major part of the mass was found to be composed of fat with irregularly disposed heavy bands of fibrous tissue. The fifth lumbar and first sacral vertebral arches were bifid. In the central part of the mass, and protruding through the bony cleft, was a multi cystic malformation in which an abnormal spinal cord terminated (Fig. 6). The defective spinal cord was divided at its termination in the mass, the cord replaced in vertebral canal, the dural envelope reconstructed, and the wound closed with silk. The postoperative course was uneventful. Three months after operation recovery was complete and normal control of the bladder and rectum has continued during the past six years.

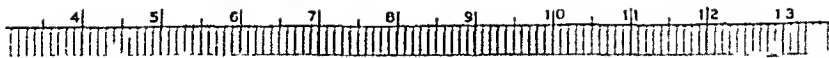
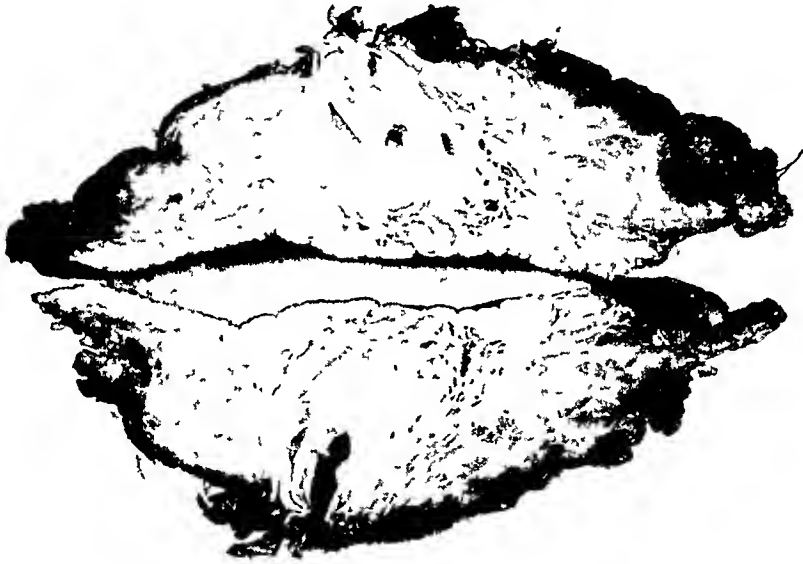


FIG 6—A fibrolipomatous mass, with an enclosed malformation of the distal part of the spinal cord removed at operation.

Comment.—The appearance of the spinal cord above the area implicated presented evidence that a normal upward migration had not occurred. The size of the fibrolipomatous mass and the cystic formation found in the vertebral canal was not such that one could assume that a direct compression of the neural elements was the causative factor of the dysfunction. It seemed unlikely that traction on the cord could account for the onset of symptoms at this late period in life. An etiologic agent could, therefore, not be assigned with certainty.

The physiology of both micturition and defecation is still not clearly understood, although some excellent work has been reported on the subject.^{18, 19, 20, 21} It seems well substantiated that the internal vesicular sphincter contracts and relaxes in reciprocal relationship with the detrusor muscle. Since the exact rôle of the three components (sympathetic, parasympathetic and somatic) of the neural mechanism of the bladder in normal man is as

ANOMALIES OF LUMBOSACRAL REGION

yet in some doubt, it is unwise to assign to each of them a particular function in disease. In an attempt to approach the problem from a clinical viewpoint, cystometric studies have been reported that appear to offer some help in estimating the exact type of pathophysiologic alterations encountered in examples of lumbosacral spina bifida.^{7, 18} McCarroll states that by careful cystometric studies all bladders can be classified according to the status of the two involuntary muscle components and of the voluntary sphincter. Such examination (cystometric) necessitates the introduction of a catheter into the urinary bladder, a procedure that is all too frequently followed by infection. The method is not applicable before the fifth to sixth year of life since cooperation of the patient is a requisite. Furthermore, it is in this younger age-group that surgical treatment frequently becomes mandatory. Therefore, an estimation of the function of the urinary bladder by other methods seems advisable. Useful information can be obtained regarding the function of the bladder by roentgenologic studies following the intravenous or subcutaneous injection of diodrast or comparable contrast media that is excreted by the kidneys.

The physiology of the bladder in any patient with urinary disturbance due to a developmental defect of the distal spinal cord may be determined by (1) observation relative to dribbling of urine; (2) the quantity of urine passed at each automatic involuntary voiding; (3) the frequency of urination; (4) an estimation of the residual urine after automatic voiding or following voluntary emptying of the bladder; and (5) the contour of the bladder before and after partial emptying. The first three of these may be readily determined, however, the last two require the intravenous or subcutaneous injection of a contrast medium that is excreted by the kidneys and the taking of roentgenograms of the urinary bladder at 15- to 20-minute intervals for a period of two hours or until urine has been passed. An additional study should be carried out immediately after automatic involuntary voiding, emptying by straining, or during overflow dribbling, both anteroposterior and lateral views being made for a record of the contour of the bladder.

CLINICAL FINDINGS

As would be expected from the anatomic description of the congenital anomalies that have been observed, no two examples are identical in their clinical manifestations. There are (a) spina bifida occulta without neural involvement; (b) spina bifida occulta with neural dysfunction; (c) spina bifida and meningocele without neural implication; and (d) spina bifida and meningocele with neural implication, or more broadly stated, spina bifida with and without myelodysplasia. Although some patients may present cutaneous evidence (hypertrichosis, telangiectasis, a dimple, *etc.*) that the underlying tissues are anomalous, most instances of so-called spina bifida occulta have been incidentally disclosed roentgenographically. Others with or without cutaneous markings and with roentgenographic evidence of a bifid state of the last lumbar and/or first sacral vertebral arch, may have symptoms (especially disturbances in micturition) that have persisted since infancy.

Occasionally symptoms have been present during childhood, then disappeared, only to recur after a number of years. Finally, there may be no complaint until the fifth or sixth decade when a slight disturbance of the urinary apparatus results in urinary retention. Some patients have mild alterations in function of the distal spinal cord throughout an active and useful life and it is only following the introduction of a diagnostic instrument into the urinary bladder or the ill-advised use of a catheter, that a chain of symptoms is initiated which frequently persists. The following report is an illustration:

Case 2.—A female, age 29, with a rounded elevation over the lumbosacral area covered with true skin, had observed since childhood that it was necessary to strain moderately to start the urinary flow. On several occasions when accidentally struck in the lower back she had "lost her water." In addition, the bowels were costive and the right foot was slightly deformed. Nevertheless, she had engaged in social activities, and for a number of years gone to business. She was married at age 24, and had had a child. For two days following delivery, there was urinary retention, relieved by catheterization. Voluntary urination was then reestablished and she was "normal" again. Following the birth of a second child, the urine was intermittently withdrawn by catheter for a period of three days, after which normal micturition was again established. This time she did not fare so fortunately. There ensued chills and fever, later intermittent retention of purulent urine and suprapubic pain. Bladder irrigations were instituted with some relief but before long there was another episode of chills and fever associated with dull aching pains in the right flank and right kidney region. It became increasingly more difficult for her to pass urine, requiring much straining even to partially empty the bladder. This patient is still in serious difficulty from the urinary tract infection, 18 months after the birth of her second child.

Comment.—The method of emptying the urinary bladder by suprapubic pressure is apparently not generally known or at least seldom employed. It should be used in all instances of urinary retention due to neural dysfunction and catheterization should not be resorted to except as a last resort. Once a pyogenic micro-organism has established itself in the urinary tract the conditions are favorable for continued growth of the bacteria in spite of all therapeutic measures.

Russell Brain²² has commented on the patient that comes under observation during adult life as follows: "In such cases (spina bifida occulta) a careful investigation of the history usually shows that symptoms were present at an early age, though improvement may have occurred, to be followed by a relapse in early adult life. Such a relapse may be due to the effect of growth in causing tension upon the lower end of the cord and cauda equina, which are anchored at an abnormally low level or to the compression of these structures by fat or by the band described by Leri." In all instances of congenital anomalies of the spinal cord encountered in adult life, especially if symptoms have been absent for several years and then reappeared, one must be on guard lest a more recently established lesion of the urinary apparatus or spinal cord be overlooked.

While the diagnosis of spina bifida occulta may be arrived at without difficulty, it is sometimes impossible to determine the exact part the anomaly may play in a child without evidence of dysfunction other than nocturnal

enuresis. Frequently bed-wetting is the only manifestation, the child being continent during the day. In all such cases conservative therapeutic measures are to be given a fair trial before any form of operative interference is carried out.

Another group of the malformations of the lumbosacral region are those with obvious protruding cystic masses covered with a thin bluish layer of epidermis or a reddish granular surface consisting of a malformed spinal cord without cutaneous protection. Usually the surface of the latter is weeping cerebrospinal fluid. The lower extremities of patients with this type of lesion are commonly distorted and the musculature of the legs and feet paretic or paralyzed. Analgesia and anesthesia of the buttocks, lateral aspects of the legs, and the feet may be demonstrable. The ankle jerks are absent. The external anal sphincter is frequently patulous. During forceful crying urine and feces may be extruded. Ventriculographic studies will frequently disclose considerable ventricular dilatation. Some of these patients require surgical repair of the spinal defect during the first few months of life lest the thin membrane of epidermis rupture and infection ensue. Furthermore, the cystic mass if untreated increases in size, thereby placing additional traction on the intradural structures. If the meningocele be well protected by relatively heavy covering, operation may be deferred until the child is ten to twelve months of age.

DISCUSSION RELATIVE TO THERAPY

In contemplating operation it is to be remembered that conservative measures are frequently ineffective and that spontaneous cures are practically never observed. The pertinent information derived from all available sources (studies of specimens obtained at autopsy, reports of observations made at operation, and theoretic concepts based on clinical findings) indicates three important factors acting singly or in combination that should be given consideration in evaluating the cause of the dysfunction associated with congenital malformations of the distal end of the spinal cord. These are (a) abnormal masses of mesodermal tissue that press upon the neural structures; (b) defective development of the sacral spinal cord itself; and (c) absence of upward migration of the spinal cord with resulting neural dysfunction dependent upon an abnormal tension being exerted on the cord. It is this traction on the spinal cord that has not been accorded its due consideration in discussions of the surgical treatment of spina bifida occulta and of the more obvious congenital malformations of the lumbosacral region.

In all instances it becomes necessary to differentiate the dribbling of urine due to a relaxed sphincter from that due to overflow incontinence, in estimating the amount of residual urine, and in determining the contour of the urinary bladder. These are basic features that must be evaluated before instituting surgical treatment in a patient with spina bifida with myelodysplasia.

There appears to be little diversity of opinion regarding the surgical treatment of simple meningoceles. These lesions are relatively rare in the

lumbosacral region. Examples have been observed at operation in which the neck of the sac was rather small and its lumen sometimes completely obliterated, there being no obvious communication between the cavity of the mass and the spinal subarachnoid space. Following careful inspection of the interior of the cyst, total excision of the meningocele will not be followed by hydrocephalus in the majority of instances. Treating the sac by rolling it up and covering the mass with a tent of fascia, as advocated by Penfield and Cone,¹¹ has not decreased the possibility of augmentation of ventricular hydrops in my experience. Masses of adipose tissue, the so-

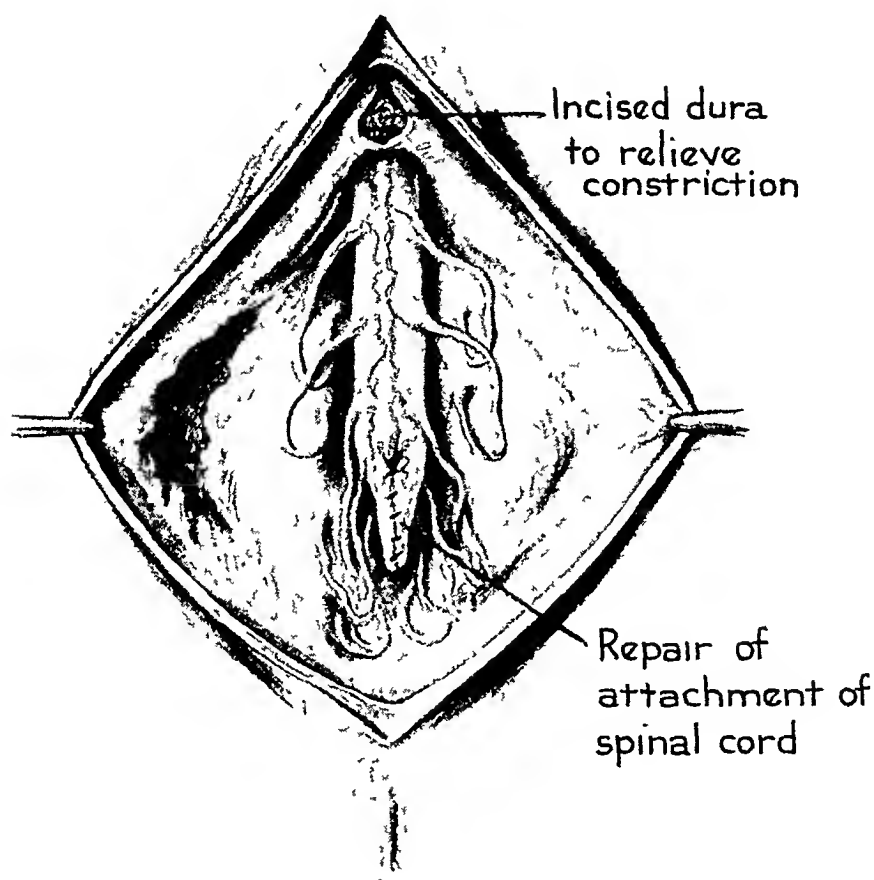


FIG 7—Illustrating the appearance of the operative field after the spinal cord has been detached from the dome of the cyst wall.

called fibrolipomata, and the "blind" meningoceles are to be well exposed and completely removed except for the fat through which spinal nerves may pass as they leave an abnormally short dural cul-de-sac.

The selection of a patient who may be improved by operative intervention is sometimes difficult. Certainly, one should not expect to correct total relaxation of the anorectal and vesicular sphincters associated with grave disorder in both motor and sensory function of the lower extremities by an operation upon a malformed spinal cord. If operation is to be carried out under these conditions it should be understood that the unsightly mass

is to be removed, so that danger of spontaneous rupture is eliminated but that the neural dysfunction will probably remain unaltered. If there be minimal motor and sensory disturbances in the legs and feet associated with analgesia and anesthesia of the saddle-area, and a spastic state of the internal sphincters, improvement in function of the sphincters, in particular, usually follows operative intervention. This has been obtained in both spina bifida occulta, where the spinal cord is adherent to the abnormal dura as well as in the meningo-myelocèles. The spinal cord distal to the point of its adherence and the nerves attached thereto are usually functionless. For this

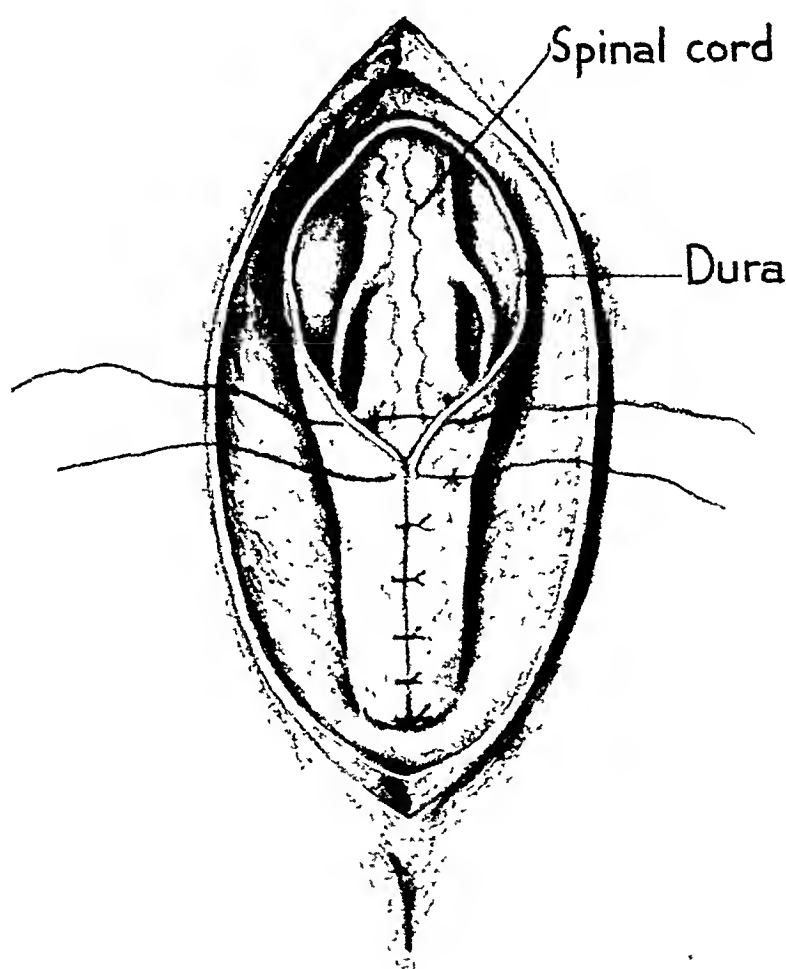


FIG. 8.—The spinal cord is lying free in the vertebral canal and a dural envelope is being reconstructed.

reason it becomes useless to attempt preservation of these structures, however, great care should be exercised to prevent damage to nerve tissue at, or cephalad to, the point of the spinal cord attachment. The incision for the exposure of the lesion should be made slightly to the side of the midline, thereby obviating possible damage to the spinal cord at its point of attachment (Fig. 4). This is particularly important in opening the cystic portion of a meningo-myelocèle. After adequate exposure and identification of all structures the cord should be freed and the cut surface closed by approximating the edges of the pia mater (Fig. 7). The cord may be found constricted

at its entrance to the sac. If so, the dura should be incised in order to relieve the constriction and a plastic repair performed to insure against recurrence of the strangulation at this site. A loose-fitting dural envelope is reconstructed, the redundant part of the sac excised and the wound closed with layer silk (Fig. 8).

Operations upon children less than 18 months of age should be performed under local infiltration of novocain. In older children and adult patients open drop ether has been employed, however, other types of inhalation anesthesia may prove just as satisfactory. The operation should be conducted with the head at a lower level than the operative field to prevent excessive loss of cerebrospinal fluid. This requirement is best met in small children by making the subject fast to a board and tilting the foot end upward. For older children and adults the operating table may be tilted to the desired position. Another item that assumes considerable importance is the prevention of contamination of the wound or the sterile drapes with feces. This is especially true in young children when the operation is being performed under local anesthesia, and the child is frequently crying. Because of disturbance in function of the anorectal sphincters fecal material is frequently extruded regardless of the care exercised in the preoperative preparation. To prevent this the anal canal is packed with cotton and the gluteal masses strapped together with adhesive tape. In addition the knees should be fixed in a fashion to keep the thighs apart. If feces is extruded it will be retained in the space between the thighs and not forced into the operative field or contaminate the drapes. At the completion of the operation in either children or adults the wound is sealed with a collodion dressing. During the postoperative period the patient should be kept on the abdomen or on the side. A cradle is placed to support the bed clothing, and diapers should not be used. The feedings need not be altered from the preoperative routine if the operation has been performed under local anesthesia. If there is evidence of increased intracranial tension this may be reduced by ventricular or cisternal puncture according to indication. Great care must be employed when introducing a needle into the cisterna magna since in some cases the medulla may have been drawn into the foramen magnum by the traction on the spinal cord and the cisterna magna thereby partially obliterated.

In the instances in which improvement in the function of the anorectal and vesicular sphincters is not obtained by the operative procedure herein described, excision of the superior hypogastric plexus should be given consideration. If all methods have failed to control the urinary and fecal incontinence and the sphincters are totally relaxed, artificial sphincters may be provided by the transplantation of the gracilis muscle.²³

RESULTS

During the past ten years 104 cases of congenital maldevelopment of the spinal cord and its coverings have been treated. In 31 of these the lesions were located in the lumbosacral region and implicated the distal part of the

spinal cord. Seventeen of these 31 patients were considered to have defects that would lend themselves to surgical treatment. There were five adults and 12 children that were subjected to operation. The oldest was age 67, and the youngest an infant of ten days. Good results were obtained in eight patients by freeing the spinal cord, as herein advocated; improvement was observed in three; one patient died of meningitis following operation, four showed no permanent changes attributable to the operation; and the remaining one could not be followed. One of the four patients, an adult considered as a failure, showed some improvement for six months after operation only to have a return of the preoperative difficulties in controlling the urine and feces. Two of the three listed as improved continue to have nocturnal enuresis although capable of controlling the urine during the day.

Among the eight patients in whom the results were considered satisfactory there were five who acquired complete voluntary control of the urine and feces after operation. Two of the remaining three resort to moderate straining to initiate urinary flow. The other one, a boy age four, who was operated upon two years ago, likewise, has some difficulty in initiating urination but has shown favorable progress during the past year. The improvement in the function of the legs and feet has not been as dramatic as the changes brought about in the control of the anorectal and vesicular sphincters. The same may be said for the analgesia and anesthesia of the saddle-area. There have been demonstrable changes for the better but no instance of complete recovery of these involved regions. It is impossible to predict with certainty at operation what the postoperative result will be, however, it may be said that the more distal the involvement of the spinal cord the better the chances for restoration of sphincteric control.

CONCLUSIONS

In a consideration of the dysfunctions attending the congenital malformation of the distal end of the spinal cord, three important factors have been discussed: First, the disturbances produced by fibrolipomatous masses encased in the vertebral canal and exerting pressure on the adjacent neural structures; second, the lack of development of the spinal cord itself; and, third, the failure of normal upward migration of the spinal cord due to adherence of the terminal part of the cord at the site of the congenital anomaly, with a resultant abnormal tension on the cord as the normal growth of the vertebral column continues. It is comprehensible how the first and second of these etiologic factors may affect voluntary control of the anorectal and vesicular sphincters and the function of the legs and feet. There are some features concerning the third factor that are not clearly understood, however, in some patients of the present series the surgical liberation of the adherent spinal cord has resulted in improvement. The operation has been described and the major steps in its technical execution illustrated. Following detachment of the spinal cord and the reconstruction of the dural envelope the resultant improvement can perhaps logically be attributed to the release of a taut cord.

REFERENCES

- ¹ von Recklinghausen, F.: Untersuchung über die Spina bifida. Virchows Arch., 105, 243, Berlin, 1886.
- ² Lebedeff, A.: Über die Entstehung der Anencephalie and Spina bifida be Vögeln und Menschen. Virchows Arch., 86, 263, Berlin, 1881.
- ³ Kermauner, F.: In Schwalbes: Die Morphologie der Missbildungen des Menschen und der Tiere. III Teil, 3, 86, Gustav Fischer, Jena, 1909.
- ⁴ Keiller, Violet H.: A Contribution to the Anatomy of Spina Bifida. Brain, 45, 31, 1922.
- ⁵ Bohnstedt, G.: Beitrag zur Kasuistik der Spinal bifida occulta. Arch. f. path. Anat., 140, 47, 1895.
- ⁶ Dittrick, R. J.: Lumbosacral Spina Bifida Occulta. Surg. Gynec., and Obst., 53, 378, 1931.
- ⁷ McCarroll, H. R.: Spina Bifida Urinary Incontinence. Surg., Gynec., and Obst., 64, 721, 1937.
- ⁸ Frazier, C. H.: Surgery of the Spine and Spinal Cord. D. Appleton & Co., New York, 1918.
- ⁹ Dittrick, R. J.: Pathogenesis of Congenital Club Foot (Pes Equino-Varus): An Anatomical Study. Jour. Bone and Joint Surg., 12, 373, 1930.
- ¹⁰ Learmonth, J. R., and Braasch, W. F.: Resection of the Presacral Nerve in the Treatment of Cord Bladder. Surg., Gynec., and Obst., 51, 494, 1930.
- ¹¹ Penfield, W., and Cone, W.: Spina Bifida and Cranium Bifida. J. A. M. A., 98, 454, 1932.
- ¹² Kolodny, Anatole: Results of Surgery in Spina Bifida. J. A. M. A., 101, 1626, 1933.
- ¹³ Coughlin, William T.: Spina Bifida: A Clinical Study, with a Report of Twelve Personal Cases. ANNALS OF SURGERY, 94, 982, 1931.
- ¹⁴ Elsberg, Charles A.: Surgical Diseases of the Spinal Cord. Paul B. Hoeber, New York, 1941.
- ¹⁵ Buchstein, H. F., and Love, J. G.: Spina Bifida Occulta. Surgery, 3, 215, 1938.
- ¹⁶ Elsberg, Charles A.: Diseases of the Spinal Cord and its Membranes. W. B. Saunders, Philadelphia, 1916.
- ¹⁷ Penfield, W., and Coburn, D. F.: Arnold-Chiari Malformation and Operative Treatment. Arch. Neurol. & Psychiat., 40, 328, 1938.
- ¹⁸ Langworthy O. R., and Dees, J. E.: A Study of Bladder Disturbances in Spina Bifida. Jour. of Urol., 35, 213, 1936.
- ¹⁹ Denny-Brown, D., and Robertson, E. G.: On the Physiology of Micturition. Brain, 56, 149, 1933.
- ²⁰ Learmonth, J. K.: A Contribution to the Neurophysiology of the Urinary Bladder in Man. Brain, 54, 147, 1931.
- ²¹ Rose, D. K.: Clinical Application of Bladder Physiology. Jour. Urol., 26, 91, 1931.
- ²² Brain, Russell: Diseases of the Nervous System. P. 560 Oxford University Press, London, 1933.
- ²³ Deming, C. L.: Transplantation of the Gracilis Muscle for Incontinence of Urine. J. A. M. A., 86, 822, 1926.

DISCUSSION.—DR. IRA COHEN (New York) expressed some surprise that out of a total of 104 cases of congenital anomalies less than one-half were in the lumbosacral region. He would have supposed that more than half would be in this location. The more common type of spina bifida is that seen in the infant, with the sac so thin that one is almost afraid that a breath will rupture it. In such a case the fear of a rupture and the development of meningitis stares the surgeon in the face, on the one hand, and, on the other hand, there is his deep desire to postpone operation, if it should be operated upon at all. This type of case presents no diagnostic problem but does offer one as to when to operate, if to operate, and exactly what type of operation should be undertaken. At times, the surgeon is forced to operate to save life. When there

seems to be a complete paraplegia, with a rectal sphincter which is obviously not under any control (it is a little more difficult to tell about the urethral sphincter), it is fair then to let the parents share the responsibility in deciding whether an operation should be performed. As to the character of the operation, Doctor Browder may be correct in his statement that excision of the sac in no way influences the future development of hydrocephalus. Dorothy Russell has reported ten consecutive cases of meningocele that came to operation, and in all there was found, at that early stage, a medulla which was crowded down into the foramen magnum and there was beginning hydrocephalus. The question must also arise as to (1) whether in addition to the hydrocephalus there is not already present at that time a deformity at the upper end of the spinal canal not necessarily due to traction, and that no matter what may be done at the lower end the patient will go on and develop hydrocephalus; or (2) should one take the stand, as Doctor Penfield does, that the sac is partly an absorbing membrane, and that in the sacrifice of this sac, rather than enfolding it, the spinal fluid circulation becomes so thrown out of adjustment that hydrocephalus will surely develop.

The other group—the spina bifida occulta—presents not so much a problem in therapy as in diagnosis. In 1918, the late Dr. Walter M. Brickner wrote a very interesting paper on the subject, presenting ten cases, five of whom had been operated upon by him. The presenting symptom in many of the cases being trophic ulceration of the extremities. Doctor Brickner brought out the point that trophic disturbances of the extremities, which are not readily explained otherwise, should lead one to think of at least the possibility of a spina bifida occulta.

DR. BRONSON S. RAY (New York) said that what may prove, in rare cases, to be the most important factor of all, is edema of the lower end of the cord at some fixed point. It is to be hoped, upon theoretic grounds, if not on the basis of experience, that in some individuals the release of this attachment alone might serve a very good purpose. As to the question of sacrificing or preserving the sac in a meningocele, Doctor Ray's experience has been very much that of Doctor Browder.

DR. JEFFERSON BROWDER (closing) said that with regard to the relative frequency of anomalies in the lumbosacral region, he had excluded instances of meningocele that occurred in the lumbar area without implication of the sacral region. The important feature of the operation for congenital anomalies implicating the distal part of the spinal cord is the release of the cord. To be sure, this is purely a theoretic concept, but Doctor Browder thought that restoration of function might be attributed to this particular operative maneuver.

THE TREATMENT OF CONGENITAL HEMANGIOMATA OF THE SKIN

LT. COMDR. GEORGE S. JOHNSON, U. S. N. R., AND RUDOLPH A. LIGHT, M. D.

NASHVILLE, TENN.

FROM THE DEPARTMENT OF SURGERY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

It is generally believed that simple hemangiomata are essentially congenital in nature. They probably have their origin, according to Watson and McCarthy,¹ in embryonic sequestrations of mesodermal tissue and grow by projecting buds of endothelial tissue.

Hemangiomata vary greatly in structure and the various types demand greatly varying types of treatment. A rigid classification is almost impossible but they may be divided into groups which overlap to a certain extent. Watson and McCarthy classify them as follows: (1) Capillary hemangioma; (2) cavernous hemangioma; (3) angioblastic or hypertrophic hemangioma; (4) racemose hemangioma; (5) diffuse systemic hemangioma; (6) metastasizing hemangioma; (7) nevus venosus or port wine stain; and (8) hereditary hemorrhagic telangiectasis.

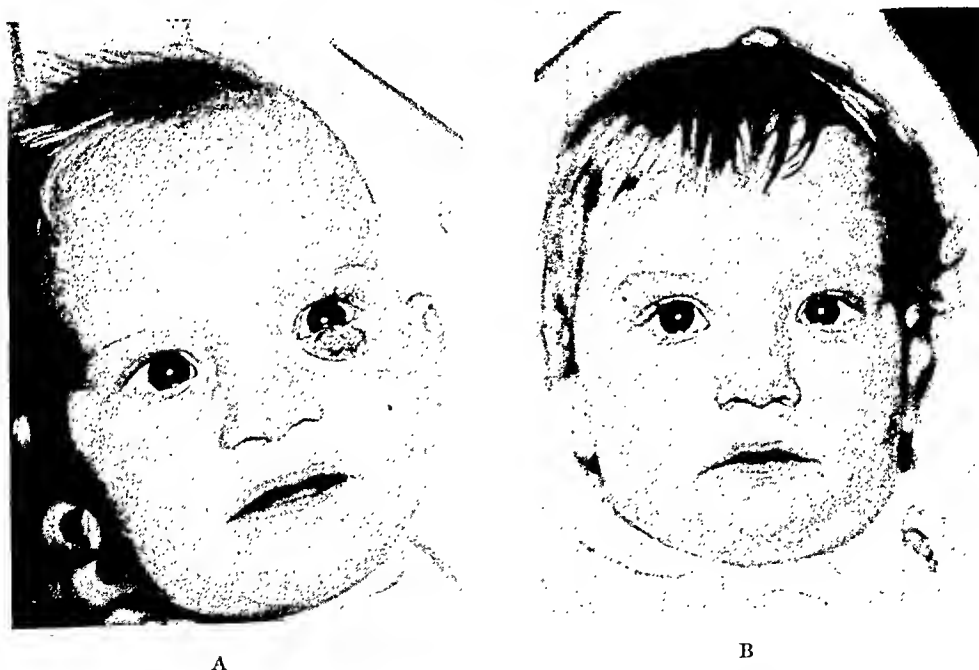


FIG. 1.—Case 1: A. Before treatment. B. After treatment.

The capillary and cavernous hemangioma and the port wine stains are by far the most frequent types. The material presented in this communication will deal with the first two types exclusively, or more correctly with capillary hemangiomata and those hemangiomata which exhibit characteristics of both types. The essential difference in these two types is in the size

of the blood spaces. Most of the deeply placed hemangioma are cavernous in type. Most of those involving the skin are essentially capillary but may be partially cavernous in type. Capillary hemangiomata are more truly neoplastic in character, they grow more rapidly and may more correctly be called hemangio-endothelioma. It is to be expected, therefore, that they be more sensitive to radiation therapy. This type of therapy when applied to the more cavernous types is essentially sclerosing in nature.

It has been pointed out by Brown and Byars,² Watson and McCarthy, and Ward and Covington³ that congenital capillary or cavernous hemangioma



FIG. 2.—Case 2: A. Before treatment. B. After treatment.

occur frequently on the head and neck and frequently involve areas where the cosmetic result of treatment is extremely important. It has also been pointed out by the above mentioned writers, and others, that these tumors may be satisfactorily treated by a number of methods with equally good results as far as curing the lesion is concerned. These methods include surgical excision, destruction by cauterization or desiccation, the use of carbon dioxide snow, the injection of sclerosing solutions, and treatment by some form of radiation. However, the results obtained by these methods may vary greatly from the cosmetic standpoint.

In those regions where excision of tissue would necessitate extensive and difficult plastic repair or where extensive scarring due to various forms of destruction would cause deformity, radiation therapy has been extensively used. This may be accomplished by the use of roentgenotherapy, the surface application of radium or radon, or the interstitial application of needles containing radium or radon seeds. Brown and Byars have emphasized the excellent results to be obtained from the use of radon seeds and also the convenience and lack of danger of the method.

The material presented herein is confined to this type of treatment alone. A series of cases is presented showing the results obtained by this method.

The technic advised by Brown and Byars has been followed as far as possible, using one radon seed for roughly each cubic centimeter of tissue irradiated, and the content of each seed varying from 0.25 to 1.0 millicurie. The amount of radon per seed depends on the size and location of the tumor. The 0.25 and 0.5 millicurie seeds are used most frequently. The 1.0 millicurie seeds are used almost exclusively in those larger tumors that are more cavernous in type.

Care has been taken to use small dosages. This has resulted in the necessity of making more than one application in several cases, but has avoided sloughing in any case, and in only one instance has there been a slight skin burn with resulting scarring.



FIG. 3.—Case 3: After treatment.

radon seeds of 0.25 millicurie each were implanted.

Picture before implantation is not available but the lesion was comparable in size to that of patient in Case 1.

Pictures show results over one year later.

Case 4.—R. L. S., colored, male, was first seen December 21, 1938, with large capillary and cavernous hemangioma of cheek, present since birth. Due to delay in hospitalization and other illness, treatment was delayed for nearly a year.

CASE REPORTS

Case 1.—W. G. A., white, male, age eight months, was admitted to Vanderbilt University Hospital, October 9, 1938. Patient had hemangioma of left lower eyelid since birth, with moderately rapid growth. On October 21, 1938, three radon seeds containing 0.25 millicurie each were implanted into the tumor. Results two years and three months later are shown.

Case 2.—R. N. C., white, female, age 12 years. Admitted, May 14, 1940, with large cavernous hemangioma of lip with capillary type hemangioma in the skin. On May 14, 1940, 15 radon seeds of 0.5 millicurie each were implanted. This did not cause total regression of the tumor. On July 15, 1940, ten radon seeds containing 1.0 millicurie each were implanted.

Photographs show patient at the age of 12, when first seen, and two years after second implantation.

Case 3.—M. L. H., white, female, age ten, was admitted, August 10, 1939, with tumor of left lower eyelid, slowly growing for several years. History of presence of tumor at birth could not be obtained. It was believed that the tumor followed trauma. On August 15, 1939, six



A B
FIG. 4—Case 4: A. Before treatment. B. After treatment

On October 28, 1939, ten radon seeds of 0.5 millicurie were implanted. Complete radiation of the lesion was not attempted or expected at this time.

On December 4, 1939, 15 seeds of 0.5 millicurie each were implanted, on December 19, 1939, ten seeds of 1.5 millicurie were implanted.

Photographs show the condition before treatment, and 18 months after the first treatment.

Case 5.—R. E. B., white, male, age 15 months. First seen June 7, 1941. Hemangioma of lip first noticed at age of three weeks. It had grown rapidly. On July 28, 1941, five seeds of 0.5 millicurie each were implanted. This obliterated the capillary part of the tumor but failed to obliterate the more cavernous part of the tumor deeper in the lip. On November 6, 1941, four seeds of 0.5 millicurie each were implanted deep in the tumor. These were implanted through the mucous membrane to prevent scarring.



A B
FIG 5.—Case 5: A Before treatment B. After treatment.

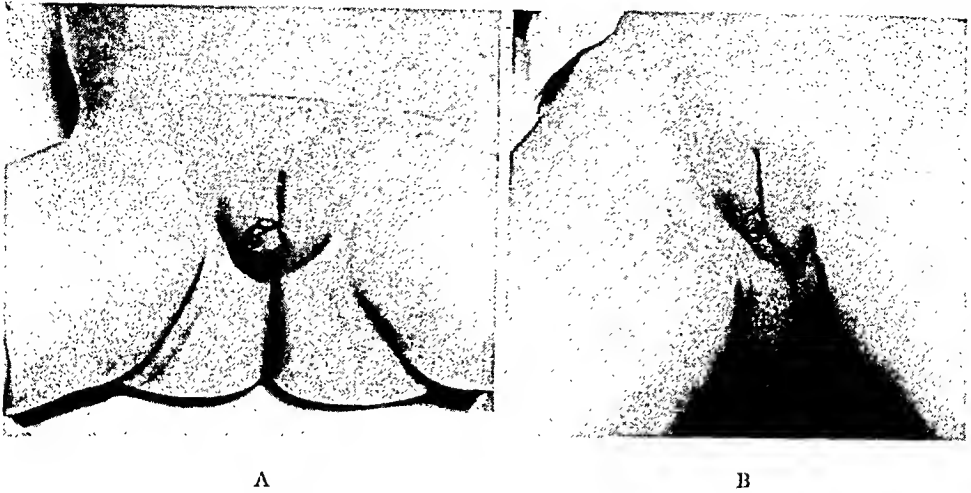


FIG. 6.—Case 6: A. Before treatment. B. One year after treatment.

Pictures show condition before treatment, and two months following first treatment. Not enough time has elapsed to note the final results of treatment.

The next two case reports are rather unusual in that they do not occur in the region of the face but on the vulva. It was thought that excision of the hemangiomata and plastic repair would be difficult and unsatisfactory, and the same type of treatment was carried out as in those occurring on the face.

Case 6.—G. M., colored, female, age two years. Hemangioma of vulva present since birth, which gradually enlarged. On October 16, 1940, ten radon seeds of 0.5 millicurie each were implanted.

Photographs show condition before treatment and result one year after implantation.

Case 7.—J. K. B., white, female, age three months. Hemangioma of vulva, present at birth, began to grow rapidly during last month.

On August 27, 1940, 15 radon seeds of 1.0 millicurie each were implanted. This

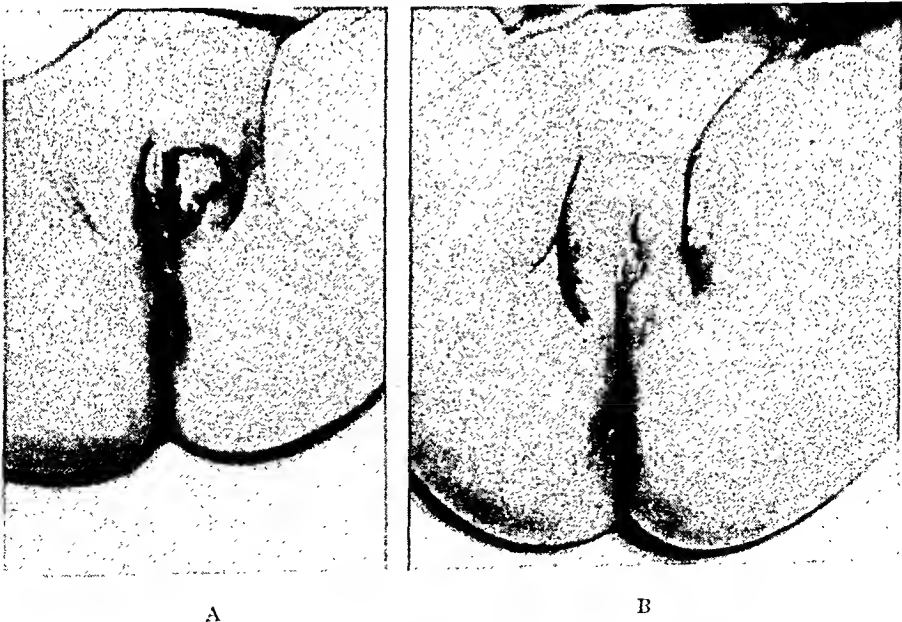


FIG. 7.—Case 7: A. Before treatment. B. After treatment.

dose was too large for this type of hemangioma. We were probably influenced by the rapidity of growth.

The patient suffered from swelling and desquamation of the vulva and has much more scarring than is necessary. There was no vulvar abscess.

Photographs show lesion before operation and approximately 15 months after operation.

SUMMARY

A brief discussion is presented as to the classification of hemangioma. The treatment of congenital hemangioma of the skin is briefly discussed, and cases treated by the implantation of radon seeds are reported.

REFERENCES

- ¹ Watson, Wm. L., and McCarthy, Wm. D.: Blood and Lymph Vessel Tumors. Surg., Gynec. & Obst., 71, 569, November, 1940.
- ² Brown, J. B., and Byars, L. T.: The Interstitial Radiation Treatment of Hemangiomata. Am. Jour. Surg., 39, 452, February, 1938
- ³ Ward, Grant E., and Covington, E. Eugene: Hemangiomas of the Skin. J. A. M. A., 114, 2069, May 25, 1940.

THE SURGICAL TREATMENT OF INTRINSIC KNEE JOINT LESIONS

FURTHER ANALYSIS OF OPERATIVE CASES

JOHN J. MOORHEAD, M.D., AND DAVID LYALL, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF TRAUMATIC SURGERY, NEW YORK POST-GRADUATE MEDICAL SCHOOL
AND HOSPITAL, COLUMBIA UNIVERSITY, NEW YORK, N. Y.

THE PRESENT DISCUSSION of this important subject is based upon experience accumulated through years of more or less constant contact with the problem. In previous communications a total of 186 operative cases were reported.^{1, 2, 3} The experience from January, 1932 to July, 1941, consisting of 189 arthrotomies, forms the basis of this communication, making a total of 375 cases cared for with basically the same operative criteria and technic as outlined by the senior author (J. J. M.), in 1932. Slight modifications have been adopted as needed but the general schema has been preserved intact. We believe that emphasis is to be placed on proper diagnosis and the understanding of definite indications for operation rather than on the actual operative technic. The surgeon must decide which cases are surgical and which require medical care alone. Of those which come into his field, he must decide which are to be operated upon and which are to be treated conservatively. Not only the presence of abnormalities but their degree of severity must be estimated in making an operative decision. A knee operated upon is never again a wholly normal joint, and hence the candid surgeon refuses to replace minor pathology by man-made defects causing equal or greater disability.

PATHOLOGIC ANATOMY

It must always be remembered, especially by the occasional operator, that the presence of multiple abnormalities is the rule rather than the exception.

Semilunar Cartilages.—The semilunar cartilages are not stationary. They move forward when the knee joint is extended and backward when it is flexed. A moment's reflection shows why this is necessary. The phenomenon is easily demonstrated on the fresh cadaver or at the operating table. The internal cartilage is approximately semicircular. It is the larger of the two and is firmly attached at its medial margin to the medial (tibial) collateral ligament. The external cartilage is smaller, nearly circular in outline and its attachment to the lateral (fibular) collateral ligament is narrower and less substantial. This is also easily demonstrable and accounts, in part at least, for the great preponderance of internal meniscus derangements. The cartilages are subject to various abnormal conditions:

1. Fracture-dislocation—the most frequent injury.
2. Dislocation without fracture.

3. Fracture without dislocation.
4. Erosions—irregularities of the cartilage surface usually encountered in the later stages of knee joint osteo-arthritis.
5. Cysts: These are of obscure origin. They usually contain a grey-yellow viscid fluid. Some are thought to be due to injury followed by mucoid degeneration, others possibly to synovial developmental inclusions.⁴ Because of their rarity they are of minor importance.
6. Developmental anomalies: These include the “discoid” cartilage which is said to be a persistence of the embryonic disk-shaped form. We have had no experience with this condition.

Synovial Membrane.—The synovium of the knee joint is the largest in the body. Because it must accommodate itself to a great variety and range of motions, it is normally loosely folded on itself. Of the entire joint structure it alone contains sensory nerve endings and hence subjective pain is expressed in terms of synovial irritation. All internal derangements are accompanied by a varying degree of synovial hyperemia and extravasation of fluid. If the irritating body is not removed this membrane becomes permanently thickened and irregular. Calcium deposits appear, and, becoming detached, give rise to multiple, small loose bodies. The late result of a chronic traumatic synovial irritation is the so-called hypertrophic or villous synovitis. Synovial adhesive bands often appear following irritation or hemorrhage. The *sub-patellar fat-pads* partake of this general synovial swelling. Frequently they enlarge to such a degree as to intrude themselves between the joint surfaces when the knee is extended. At operation, the tips show a characteristic reddened “pinched” appearance and they also may eventually become calcified and detached, giving origin to a loose body.

The *joint surfaces* of the knee undergo progressive changes, which may be thought of as due to wear and tear. This degeneration is hastened by overweight, by overuse, or by the continued presence of loose bodies or other joint irritants. In general, the changes are indistinguishable from an *hypertrophic osteo-arthritis*, characterized by irregular bony overgrowth and marginal osteophyte formation. *Osteochondritis dissecans* is an obscure condition in which a fragment or fragments of cartilage and underlying bone are detached from a joint surface. In the knee the source is usually the mesial articular margin of the internal femoral condyle. The detached fragments then become loose bodies and their continued presence cause the usual secondary changes. It is said that the medial condyle of the femur can be injured by the medial meniscus when sudden backward pressure is brought on the hyperextended knee.⁵ This is a separate entity and probably should not be confused with osteochondritis dissecans.

Calculi of indeterminate origin are frequently found. They are different from the joint mice of osteochondritis dissecans because they are smooth and convex on both sides while the latter usually have a rough, concave side corresponding to a defect on the femur. Locking may be the first symptom of their presence.

Diagnosis.—By far the most important single aid in achieving the proper understanding of any particular case is the *history*. This should include a minute and exact catechism on the mode of injury and subsequent course. One should convince oneself as to the *adequacy* of the alleged trauma. It is also important to accurately understand descriptive terms as applied by the layman. For example the term “locking” is often used to describe *difficult* extension of the knee due to pain, whereas, actually, it should mean an insurmountable wedging of the joint. This is a very important distinction.

Mode of injury is often difficult to determine and may be buried in the dim past. In our series of cases, the average interval between the first connectable injury and operation is somewhat less than 27 months. The earliest case was operated upon one week after trauma, while the longest elapsed time was 50 years. Ferguson and Thompson,⁶ reporting 100 cases, state that the average time from injury to operation was two and one-quarter years, which nearly exactly corresponds to the time-interval in the present series. The most common type of violence is a “twisting” or “wrenching,” with the affected knee in a partially flexed position (42 per cent of our cases). Direct violence to the knee without twisting or wrenching was mentioned in 16 per cent of our cases, and an equal number gave a history of a “fall,” without definite recollection as to the mode of injury. Fifteen per cent gave no history of trauma whatsoever and, of these, spontaneous locking was the presenting symptom in two cases. A small group (seven per cent) gave a history of locking of the joint on arising after prolonged kneeling, stooping or sitting. Another small group consisted of cases of severe injury about the knee (2 fractured femora, 1 fracture of patella, 1 dislocation of knee) in which the cartilage injury became apparent only after the major damage had been repaired. One case had been injured by a bullet, and another by a retained foreign body.

TABLE I
MODE OF INJURY

	Per Cent
Twisting or wrenching violence.....	42
Direct violence, without knowledge of fall or twisting ..	16
Fall, without definite knowledge of mode of injury.....	16
No history of trauma.....	15
Locking of knee following prolonged stooping or kneeling ..	7
Internal derangement masked by major fracture or dislocation	3
Foreign body and bullet wound (one case each).....	1
Total.....	100

Following the original injury a varying amount of swelling, pain, and stiffness supervenes. It usually regresses in two or more weeks, and the patient may have only minor difficulty for a long time, characterized by a vague feeling that the knee “is weak” or that it “doesn’t feel right.” The history often becomes one of repeated minor mishaps followed by pain, limitation of motion, or knee joint effusion. Locking may appear early or late. It is a capricious but important symptom. Frequently the patient complains of “clicking” or “grating” sensations, especially on forceful extension of the

joint, as on climbing stairs or arising from a chair. Weakness and "giving way" of the knee become especially frequent on going downstairs. The location and character of pain is carefully noted. Occasionally a loose body in the joint will be felt by the patient and demonstrated at different points in its peregrinations around the knee. Loss or gain in weight is always of importance in evaluating the capabilities of a knee joint. Finally, it is of utmost importance to inquire into the bleeding tendencies of a prospective operative patient and, if necessary, to determine the bleeding and clotting time.

Physical Examination.—Adequate exposure is insisted upon. One observes particularly the gait and the presence or absence of muscle atrophy, especially of the quadriceps group. A markedly atrophic thigh makes a poor operative risk, and insures a slow, unsatisfactory postoperative course. Comparative measurements of girth at certain levels can be made and recorded for future reference. Limitation of active and passive motions is determined—always bearing in mind the rôle of pain and voluntary muscle spasm.

When swelling is present, one should determine whether it is due to fluid or to synovial thickening, or both. The rim of the tibial plateau is explored carefully with the knee in both flexion and extension. In this way, telltale tenderness or small irregularities are discovered.

Crepitation is often best observed with the palm of the hand on the patella while the joint is opened and closed. Variations can be estimated audibly by means of the stethoscope, and, with the practice attained by making such an examination a routine, information of value is obtained.

Roentgenologic examination is a routine in all operative cases and in those in which there is a history of trauma. As in a great many other locations, the positive film is of considerable value but an entirely negative film is of somewhat lesser importance. Operative decisions, in general, are made from clinical criteria. The knee is taken in three views—(1) anteroposterior; (2) lateral; and (3) postero-anterior. The technic and posturing are shown in the accompanying diagrams (Figs. 1, 2 and 3). A fourth view is very occasionally used (Fig. 4). Obviously, the marked degree of flexion necessary will be impossible to obtain in most cases. It silhouettes the femoral articular surfaces and the under surface of the patella. In the three routine views note that the central ray beam is always parallel to, and just above the tibial plateau.

GENERAL CONSIDERATIONS

This series of 189 knee joint arthrotomies was performed upon 170 patients. Fifteen patients were operated upon twice, and one patient no less than five times (for rapidly recurring pain and disability due to osteo-arthritic spurs and hypertrophic synovitis, with calcification and multiple foreign body formation). There were 137 males and 33 females. The average age was 33.7 years (males, 32.8; females, 37.3 years). The oldest was 67 and the youngest 13. One hundred forty-seven arthrotomies were performed

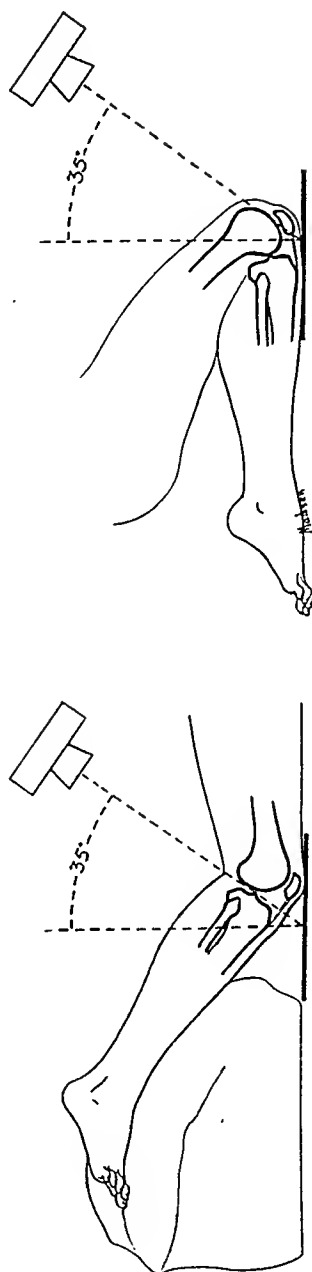
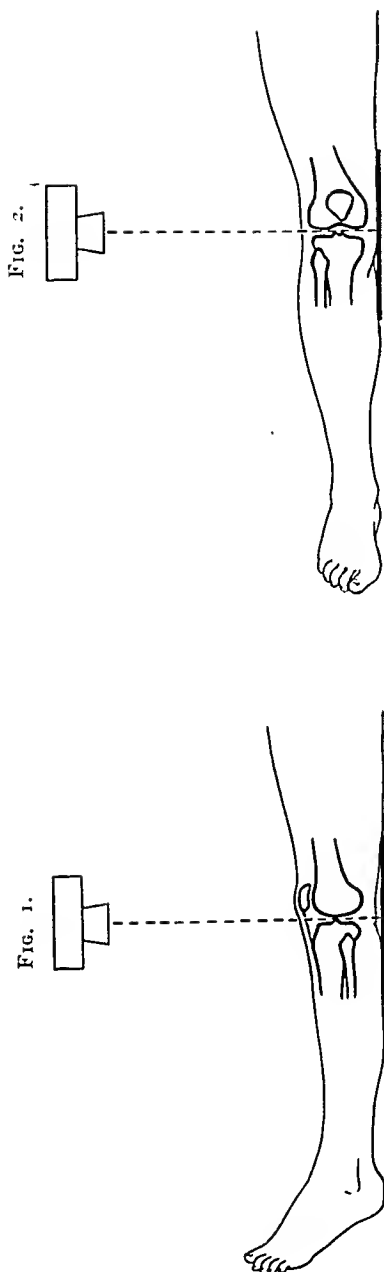


FIG. 1.—Routine anteroposterior view.
FIG. 2.—Routine lateral view. The knee is flexed about 30° .
FIG. 3.—Routine postero-anterior view. Foot supported by pillow. This opens intercondylar notch.
FIG. 4.—Optional view. Limited use. Sometimes of value in demonstrating abnormalities missed in routine roentgenograms.

upon males: 42 upon females. In the males the great bulk of patients were between the ages of 20 and 35 and, on the whole, were an active, healthy well-developed group consisting chiefly of workmen and exathletes. One hundred three (70 per cent) of the males had frank cartilage derangement. Ten (seven per cent), presented severe meniscus erosion, necessitating removal. Eight (five per cent) showed typical osteochondritis dissecans, with loose body formation, and six (four per cent) contained loosed bodies (calculi) of doubtful origin. The remaining group of 15 (14 per cent) consisted mostly of hypertrophic osteo-arthritis, with a sprinkling of rarer conditions. A survey of the females operated upon showed that less than one-half presented cartilage injuries. These appeared mostly in younger women and girls injured in sports. As the average age of the females was higher than that of the males, one would expect a larger percentage of hypertrophic osteo-arthritis. Such was the case.

The *differential diagnosis* of surgical lesions of the knee joint is best made if the above factors are kept in mind while making the routine examination.

Derangement of the Cartilages.—This is the most common erroneous diagnosis. A typical history of injury with locking followed by joint effusion and joint tenderness *directly over* the internal meniscus is not always obtained. In our experience, definite locking was present in about one-half of the cases of proven cartilage derangement. It is not a necessary symptom. The exact figure is hard to arrive at. So-called "bucket-handle" fracture (detached except at either end) was the most consistent cause of locking (75 per cent of the time). Other proven cases of cartilage derangement, plus loose bodies in the form of calculi and the remnants of osteochondritis dissecans, caused locking in only one-half the cases. It is interesting to note four cases of locking in which no loose bodies of any kind were found. These may have been occasioned by temporary abnormal mobility of the cartilages.

In acute cases *roentgenograms* usually show only capsular distension, with a floating patella. Narrowing of the joint space on the side of the deranged cartilage, as seen in the anteroposterior exposure has not been a common finding in our experience. Sprain of the internal collateral ligament of the knee is to be differentiated by location of maximum pain and tenderness about one inch above the cartilage level over the medial condyle of the femur. The external meniscus derangement (only four cases in this series) is diagnosed with difficulty. Tenderness over this cartilage is usually misleading.

Knee joint calculi and loose bodies associated with osteochondritis dissecans often appear without alleged trauma (although some knee injury usually can be recalled by anyone, if sufficiently interrogated). The migrating offender may be felt in the quadriceps pouch or may appear and disappear at various locations on the periphery of the joint. Roentgenograms visualize these types of loose bodies if they contain sufficient calcium or if not ob-

scured by superimposition of dense bony shadows. In the case of osteochondritis dissecans careful roentgenologic study, in various oblique views, may reveal an irregularity of bony contour in the region of the lateral aspect of the medial condyle of the femur.

Hypertrophic synovitis and hypertrophy of the subpatellar fat-pads are to be expected as sequelae to long-standing intrinsic knee pathology, particularly those conditions causing repeated traumatic synovitis with bloody or serous extravasation. Enlarged fat-pads may interpose between the femur and tibia when the knee is brought to extension. In such a case, continued extension meets relative, not absolute resistance, and is painful but not impossible. This is not *true* locking.

Hypertrophic osteo-arthritis is evidence of wear and tear on the knee joint. Typical joint changes, with spur formation, occur, due to untreated joint calculi after many years' trouble and are monarticular. *Both* knees are involved as part of a generalized osteo-arthritis, which manifests itself in one or both joints due to increase in weight, postural defects, or other situations which result in abnormal or overuse. An advanced degree of arthritis may be present for years and never manifest itself until one of these precipitants occurs. These joints develop considerable limitations of motion, with or without severe pain. At times, crepitations due to destruction of cartilaginous bearing surfaces becomes so loud as to be heard across the room.

TREATMENT

Nonoperative.—This is often the lesser of two evils, and is carried out by the conscientious surgeon in the face of many importunings to be more radical. Emergency arthrotomy is never employed except in the presence of irreducible locking. Points to be emphasized in a conservative therapeutic regimen are:

1. *Weight reduction* undertaken slowly and carefully, with proper attention to vitamin intake and avoidance of debility.

2. *Posture.*—This includes special instruction in proper walking and particularly to correct pronated, weak feet. The patient should attempt to toe-in, and bear the weight on the outside of the foot. A lift (one-quarter-inch) on the inside of heel and sole often helps to readjust the weight-bearing axis. Foot exercises for muscular strengthening are of value.

3. *Exercises.*—It must be remembered that of all of the muscles of the body the quadriceps femoris atrophies the quickest. Hence, the emphasis is on early, active repetitive motions to maintain this important muscle. No knee is stable or safe from future debacles if activated by a weak or flabby quadriceps. "No knee is stronger than its quadriceps."

4. *Aspiration.*—This is carried out with careful attention to sterility. In fresh injuries a sanguineous or serosanguineous fluid is aspirated, whereas later the fluid is found to be straw-colored and more viscid. Following aspiration the joint is firmly bound with a three-inch bandage of the ACE-

type. Remarkable relief of pain sometimes occurs when a tense capsule is decompressed.

5. *Physiotherapy*.—Baking and massage are of considerable aid in relieving the swollen, painful joint. The indiscriminate use of short-wave diathermy, and allied modalities, is to be condemned. These impressive machines tend to take the place of thought on the part of the surgeon and effort on the part of the patient. Certainly, it is unwise to attribute to them any specific virtue.

Operative Intervention.—This is chosen only after a reasonable amount of conservative treatment has been unavailing. Operation is undertaken for persistent or recurring disability due to internal derangements and for recurrent locking. In these cases one must not wait too long before operating because irreversible changes take place. Such secondary developments as hypertrophic synovitis, osteo-arthritis, or enlarged subpatellar fat-pads are only partially remediable. One occasionally operates with the specific idea of prophylaxis but, of course, only when the diagnosis is definite.

Unfortunately, many patients refuse surgical intervention, preferring to temporize with minor, but ever increasing disability. They are to be seen painfully limping, often with flexion contractures and in the end stages of joint destruction. But even here, if the musculature is capable of pre-operative activation and with complete cooperation on the patient's part, one can hold out, tentatively, some relief from an operative "cleaning out." Likewise, selected cases of recalcitrant hypertrophic osteo-arthritis, unassociated with trauma, can be operated upon, but, again, the potential rehabilitation must be envisaged. The question of excision of the patella will be briefly taken up below.

Preoperative Preparation.—The patient is admitted the afternoon of the day before operation. The entire thigh, leg and foot is shaved, washed thoroughly with green soap followed by alcohol and then ether. It is carefully wrapped in sterile dressings which are kept wet with a solution consisting of four cubic centimeters of tincture of iodine to 500 cc. of saline. Bleeding and clotting times are determined where indicated—this could probably be made a routine, with profit. A light cathartic is administered in the early evening and followed, if necessary, by a low saline enema the next morning.

Choice of Anesthesia.—Morphine and scopolamine are administered one hour preoperatively as a routine. The usual case is handled readily by a low spinal anesthesia, since about one hour is the elapsed time from the application of the tourniquet until its removal. Avertin-gas-oxygen-ether sequences or cyclopropane are frequently employed when the patient is of an apprehensive type.

Operative Technic.—This has been described at length elsewhere.^{1, 2} An Esmarch bandage is wound tightly while the leg is elevated, to render it bloodless, and the tourniquet applied to the upper thigh, making sure that the femoral vessels are well padded. The tourniquet should not be used

in the presence of advanced arteriosclerosis or peripheral vascular disease. None of our cases were denied its use. The patient lies supine on the table. Draping of the extremity is carried out so that complete mobility is possible without restriction. Rigid Lane-technic is adhered to throughout. This includes additional precautions in the preparation of the operative field, a general "hands off" policy, and the sterilization of each instrument after each operative step. Suture material is handled only with instruments. No vessels are ligated.

Type of Incision.—Many ingenious approaches to the knee joint have been devised. All have certain disadvantages. The split-patella approach gives excellent exposure but seems unnecessarily mutilating. Besides, it requires a postoperative plaster of paris casing. Moder⁹ make a U-shaped central skin incision and turns the skin flap upwards. The patella tendon is split vertically and the patella dissected out. This also would give excellent exposure but we believe routine excision of the patella to be unnecessary. The incision used by Haggart and Touney⁸ involves the turning of a medial skin flap. Following this, the joint is exposed *via* two vertical incisions—before and behind the internal lateral ligament. It permits removal of the entire medial meniscus but wide exploration would not appear to be possible. We continue to employ the mediolateral incision because it permits wide exploration and early, active mobilization. We believe that in the rare, early case a short (three-to-four-inch) incision can be made, always with readiness to enlarge it. In all recurrent or late cases the incision is made long enough, usually five to seven inches, to permit dislocation laterally of the patella. This permits wide exploration, visualizing both menisci, the character and contents of the quadriceps pouch, and the under surface of the patella. Surgical attention to enlarged fat-pads, synovial and bony excrescences is readily given. As in abdominal surgery, one operates with a definite diagnosis in mind but continues the analogy to the knee in maintaining that exploration is part of the "celiotomy" of the knee joint.

ANALYSIS OF CASES

Of 189 cases operated upon the internal meniscus was removed in 139 (74 per cent). In addition, three cases, previously operated upon elsewhere, showed sizeable remnants amounting to perhaps half of the cartilage. These were removed with relief of symptoms. Of the 139 cases subjected to removal of the internal cartilage, 121 showed evidence of fracture or dislocation, or both. About one-third of these (36 per cent) showed the "bucket-handle" deformity. Seventeen cartilages were removed because of marked "erosions"—irregularities associated with other changes in the joint. One cartilage was removed because of cyst formation.

The external cartilage was removed a total of eight times—four times for frank injury, and four times for "erosions."

Hypertrophy of the subpatellar fat-pads was of sufficient degree to require removal of 64 cases. Partial synovectomy was carried out in 61 cases. Loose

bodies of all types were removed in 26 cases, varying in size from the tiny "rice-bodies" to almond-sized or larger calculi. Bony spurs and irregularities were removed in 21 cases. In seven cases bony defects corresponding to the location of an osteochondritis dissecans were found and smoothed off. To those who advocate the buttonhole exposure of the knee joint the following is of interest: Of the 121 cases of frank cartilage injury, other abnormalities (of the synovium, fat-pads or bony structures) of sufficient degree to warrant surgical attention were found in 77 (64 per cent). Most of these defects would not have been seen, let alone remedied *via* the small incision. The sole objection to the long incision is the length of the scar. However, in our experience, healing occurs with rapidity and safety.

In three cases of far advanced hypertrophic osteo-arthritis the patella was removed. In two of these the patella had become fixed to the femoral condyles causing marked limitation of motion. The other case presented extreme destruction of articular cartilage. Motion was painful, slow, and accompanied by a hair-raising "scream" audible across the room. At operation, it was found that deep grooves had been gouged on the femoral surface by the offending patella. In another case of far-advanced hypertrophic osteo-arthritis, arthrodesis was performed for relief of pain.

There was one cystic protrusion into the joint, apparently arising from the synovium over the external lateral ligament. In another case, a similar excrescence was found growing from the anterior cruciate ligament near the attachment of the medial meniscus. One arthrotomy was performed to remove a darned needle which had worked its way into the joint.

Postoperative Treatment.—A large "muff"-dressing, consisting of several layers of sterile absorbent cotton, is firmly applied from mid thigh to mid-calf before the tourniquet is released. Snugness is obtained by bandaging over the cotton with several layers of five-inch muslin. The patient is put to bed with the extremity elevated on one or two pillows. The following day a cradle is installed to support the bed clothes and to facilitate exercises. For warmth a 60-watt bulb is kept under the clothes, although this may not be necessary in summer time.

At the earliest possible moment exercises are begun—usually from 36 to 72 hours postoperative. The first maneuver is for the patient to reeducate the quadriceps by "shrugging" the patella. It may take a day or two for some patients to regain the ability to contract the quadriceps while others begin immediately. Often, in face of pleas of pain, a forceful demeanor is necessary to secure cooperation on the part of the patient. The next step requires him to lift the extended leg off the bed. This can usually be done in three to seven, occasionally more, days. The patient is allowed in a wheel chair on the 4th or 5th day. Sutures are removed on the 7th to 10th days, and the patient encouraged to walk. He pushes a chair ahead of him at first and, when able, graduates to a cane. Crutches are not used.

Systematic, repetitive exercises, designed to use the quadriceps muscle and bend the knee, are performed daily, until atrophy is no longer present. Swim-

ming is an excellent exercise of this type, particularly the so-called "crawl" kick. After the leg can be raised with ease the opposite or "good" leg is laid across it and its weight added to that of its mate. Later, forceful resistance can be applied. For office workers and people at home, placing a waste basket over the foot, with or without weights, increases the effort necessary for extension.

Postoperative *aspiration*, routinely proposed by some,⁷ we use exceedingly rarely. Physiotherapy is employed in the form of baking and massage daily or three times a week until adequate motions are restored. The whirlpool bath is of great help in selected cases. However, it must be emphasized that nothing takes the place of conscientious muscular effort on the part of the patient. The office worker returns to work in four to six weeks. The laborer may require six to eight weeks, and in some of the more perilous callings even more.

Postoperative Complications.—There was one case of gross joint *infection*, eventually necessitating a mid thigh amputation. During an acute postoperative mania this patient tore off his dressing and had to be transferred to a psychiatric hospital. A second case was discharged with apparent primary union. One month postoperatively, redness and heat in the wound led to abscess formation, necessitating drainage. The joint space was not involved nor was the final result compromised in any way. No other infections occurred. *Hemorrhage*: In one case, wound healing was delayed by hemorrhage with clot formation. The wound was reopened down to the synovium, cleaned and resutured. Excellent healing was obtained. There were no deaths, nor were there any severe pulmonary complications in this series.

Results.—Uniformly good results are anticipated in cases of cartilage derangement, loose body formation or other nondegenerative situations where the patient is young or in early middle age and secondary changes of an irreversible nature have not yet supervened. The importance of pre- and postoperative quadriceps activation is to be emphasized.

In the series operated upon for relief of pain and disability due to advanced osteo-arthritic changes, with or without hypertrophic or calcific synovial changes, only about one-half achieve permanent improvement of substantial degree. The rest generally show improvement for six to twelve months, when progressive changes again evidence themselves. Patients will sometimes beg to be operated upon again, as in the one case in which revision was undertaken four times on the left and once on the right side in a period of four years. Each time symptoms returned after about six months relief. In this regard the subject of excision of the patella comes up. The status of this procedure has not yet been established and, certainly, our three cases are not enough to allow any conclusions to be drawn. We note, however, that the deformity due to change in contour is almost unnoticeable. It has been said that one of the functions of the patella—since it lies mostly beneath the patellar tendon—is to keep the pressure of the tendon from impinging

on the synovial membrane overlying the anterior femur. It is reasoned that a slightly inflamed synovium will cause painful motion if the suspensory action of the patella is removed. We have had no definite indication that this is the case. Of the three cases, one obtained an excellent painless knee. In one, motion and function were restored, but after six months pain and disability recurred. The third case obtained freedom from pain and greatly increased motion but shows marked weakness in extension, due apparently to separation of some of the central fibers of the patellar tendon.

SUMMARY

1. One hundred eighty-nine knee joint arthrotomies are added to previous reports, making a total of 375 cases.
2. Nonoperative methods and criteria for operations are discussed.
3. Operative routine used includes: (a) Meticulous preparation; (b) use of tourniquet; (c) careful Lane-technic; (d) use of mediolateral curved incision of length adequate for exploration; and (e) tight "muff"-dressing.
4. Postoperative routine emphasizes early active motions.
5. Complications consisted of: (a) Two infections—one following an acute mania, during which the patient tore off his dressing; the other occurring one month postoperative, after apparent uneventful healing; and (b) hemorrhage in one case, necessitating resuture of the wound, without impairing the final result.
6. End-results, and their anticipation, are discussed.
7. Removal of the patella in cases of advanced osteo-arthritic changes is briefly considered.

REFERENCES

- ¹ Moorhead, J. J.: Arthrotomy for Knee Joint Calculi. *ANNALS OF SURGERY*, 83, 392-410, March, 1926.
- ² Moorhead, J. J.: Knee Joint Arthrotomy. *ANNALS OF SURGERY*, 96, 17-26, July, 1932.
- ³ Moorhead, J. J.: The Surgical Knee. *South. Surg.*, 1, 131-140, July, 1932.
- ⁴ Willard, F. P., and Nicholson, J. T.: Cysts of Semilunar Cartilages. *ANNALS OF SURGERY*, 112, 305-309, August, 1940.
- ⁵ Smith, A. DeF., and King, B. B.: Injury to Femoral Articular Cartilages by the Medial Meniscus. *Surg. Gynec. and Obst.*, 71, 670-683, November, 1940.
- ⁶ Ferguson, L. K., and Thompson, W. D.: Internal Derangements of the Knee Joint. *ANNALS OF SURGERY*, 112, 454-470, September, 1940.
- ⁷ Bohlman, H. R.: Semilunar Cartilages: Improved Technique for Removal and Postoperative Treatment. *J. A. M. A.*, 115, 2243-2246, December, 1940.
- ⁸ Haggart, G. E., and Toumey, J. W.: Knee Joint Arthrotomy for Removal of Semilunar Cartilage: Technique of Lateral and Anterior Incisions. *Surg. Clin. N. Amer.*, 19, 709-714, June, 1939.
- ⁹ Moder, V. O.: New Approach to the Knee Joint. *Can. M. J.*, 42, 17-18, January, 1940.
- ¹⁰ Darrach, W.: Internal Derangements of Knee. *ANNALS OF SURGERY*, 102, 129-137, July, 1935.

A LIGHT, COMPACT UNIT FOR THE INTRAVENOUS OR INTRA-OSSEOUS INJECTION OF PLASMA IN EMERGENCIES

ALISON H. PRICE, M.D., AND LEANDRO M. TOCANTINS, M.D.

PHILADELPHIA, PA.

FROM THE DEPARTMENT OF MEDICINE, JEFFERSON MEDICAL COLLEGE, PHILADELPHIA, PA.

THE PRESENT FORMS of apparatus for administering plasma are heavy, expensive, bulky to transport, complicated to set up, require a standard or upright, and the overall time of administration is long. Figure 1 compares the weight and size of the units now in use with our compact container.

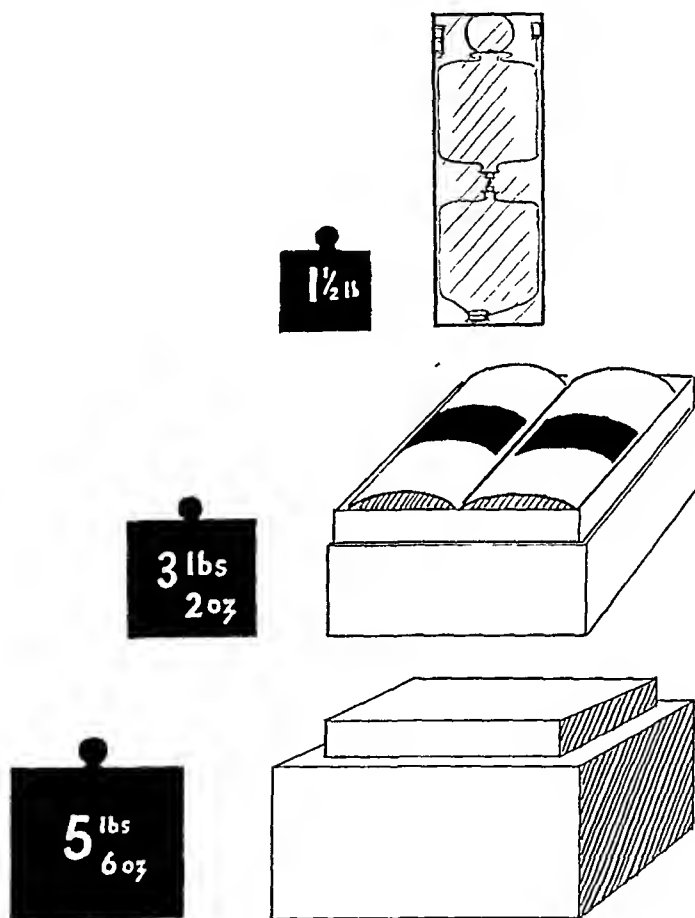


FIG. 1.—Comparison of the weight and size of described unit (1) with two other units now available (2) and (3), all containing approximately the same amount of dried plasma.

Under conditions of warfare, with the ever present menace of casualties among combatants and the civilian population, there is need for a small, compact, lightweight, durable, refillable unit by which plasma can be administered rapidly under adverse and ideal conditions.

Previously described units^{1, 2} are not designed for the emergency admin-

INJECTION UNIT FOR PLASMA

istration of plasma to those patients whose circulatory depression is so marked that it is difficult or impossible to introduce anything into their circulation by the venous route. It is at this time that fluids are most urgently needed and the intra-osseous route should be used.³ With the simplified apparatus here presented, for injecting plasma rapidly into the acutely disabled patient, it is possible to administer 16 to 20 grams of plasma (dry weight) intravenously or intra-osseously within five minutes after beginning operation. The average time is four minutes.

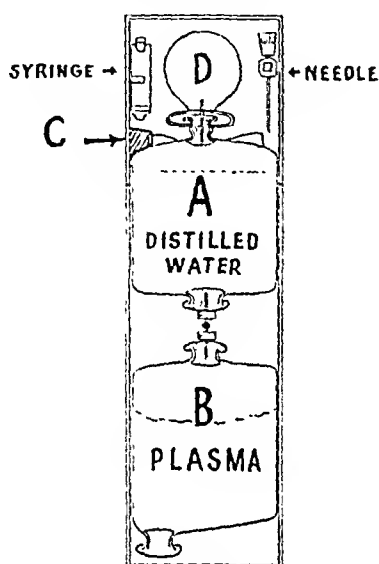


FIG. 2.—Arrangement of the unit: A. Distilled water bottle. B. Plasma bottle. C. Retaining flange. D. Rubber pressure bulb.

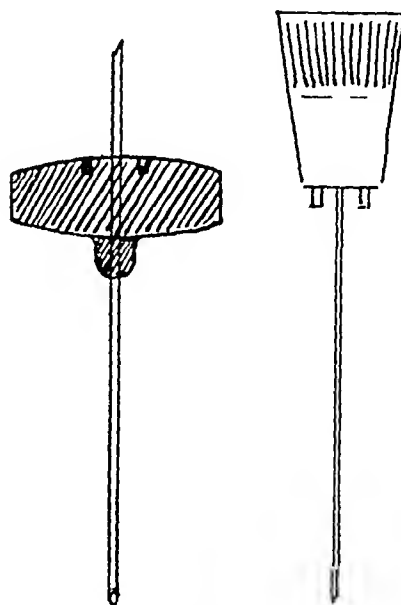


FIG. 3.—Dual-purpose needle with the stylet removed.

The unit (Fig. 2) filled and packed for transit weighs 680 Gm. ($1\frac{1}{2}$ pounds). The complete apparatus measures 22.5 cm. ($8\frac{3}{4}$ inches) long x 6 cm. ($2\frac{5}{16}$ inches) in diameter, and can be packed in a metal can under vacuum. The diameter of the container is comparable with the average water glass and is easily held in the hand. The dual-purpose needle and the syringe are mounted in the upper cover. In use, no part of the apparatus need be laid aside; it can be operated without any accessory equipment or aid. The entire amount of fluid may be given without danger of administering air, as the lower end of the bottle is tapered and the transparent cylinder makes the plasma level visible during the entire administration.

The unit (Fig. 2) is composed of two 120 cc. pyrex glass bottles, with openings at both ends. Mobile Bottle A, containing 100 cc. of sterile pyrogen-free water with 0.1 per cent sodium chloride, rides in key-way when top cover is removed. The flange (C) in the upper cover holds the winged-arms of the upper bottle and prevents rotation and motion during transit or handling. Fixed Bottle B contains 16.5 grams of desiccated human plasma representing 250 cc. of original liquid pooled plasma. This dried plasma is packed under vacuum of 73.6 cm. (29 inches) Hg. The bottles are mounted in a metal, fiber, or transparent plastic case which holds them securely. The

FIG. 4.

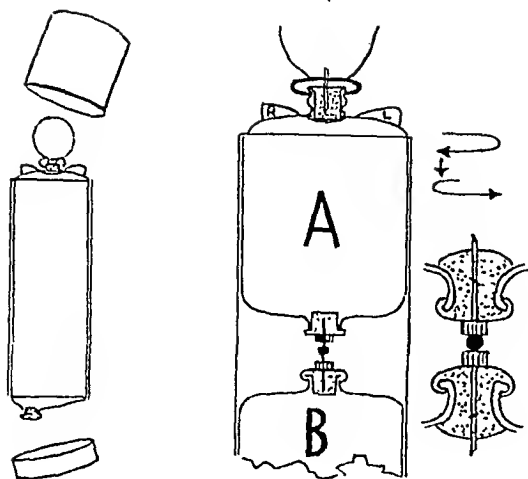


FIG. 6.

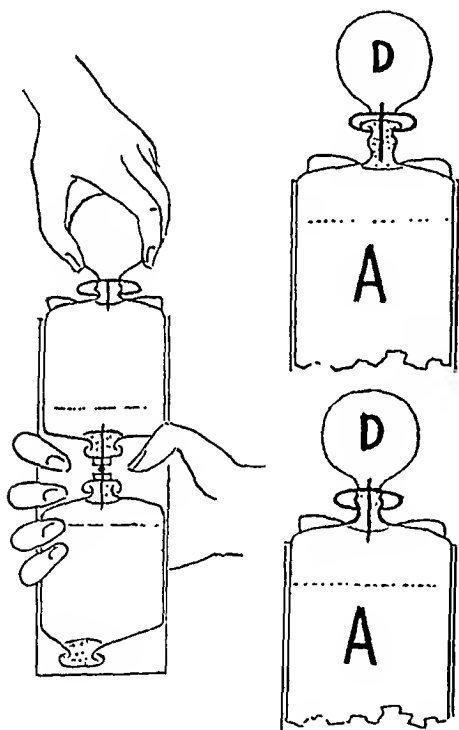
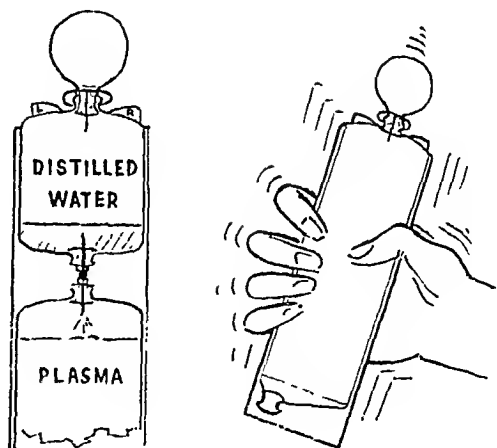


FIG. 5.

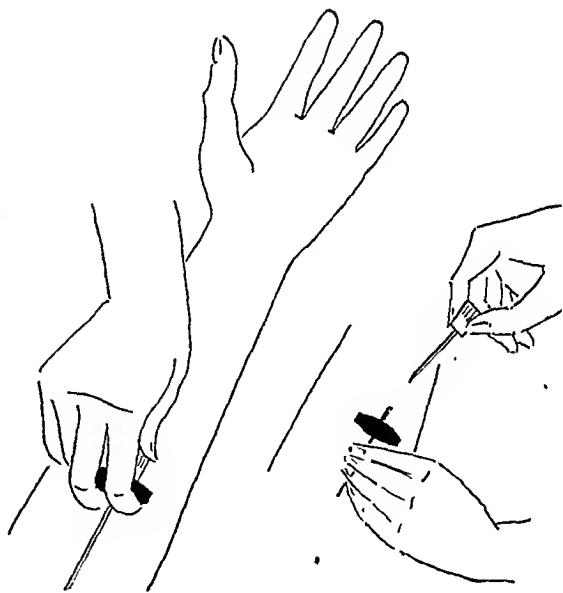


FIG. 7.

FIGS. 4-7.—Steps in the technic of administration of plasma intravenously. (Remaining steps illustrated on page opposite.)

clearance between the pyrex bottles and the plastic covering is $\frac{1}{64}$ of an inch; this prevents damage to the contained bottles if dropped or jarred. All four openings are covered with hood-type neoprene or rubber stoppers. A double-pointed needle of gauge No. 18 is suspended between the two bottles so that the downward movement of the water bottle A results in puncture of the central stoppers of the water bottle and the plasma bottle. When ready to restore the plasma to the liquid state the rubber bulb D (with cotton filter) is pushed home, the metal clip catching over the flange of the water bottle. The vacuum in the plasma bottle causes the distilled water to flow from

INJECTION UNIT FOR PLASMA

bottle A into bottle B. If, for any reason, all the distilled water fails to go into the lower bottle, it can be forced in by compressing rubber bulb D. The entire unit is then shaken until the plasma is completely in solution.

The dual-purpose No. 16-gauge needle (Fig. 3) is made of stainless metal and has the 3 mm. bevel parallel to the winged-arms, thus, facilitating intravenous insertion. The winged-arms and the tapered stylet-head allow better purchase, aid in the intra-osseous insertion, and facilitate the removal

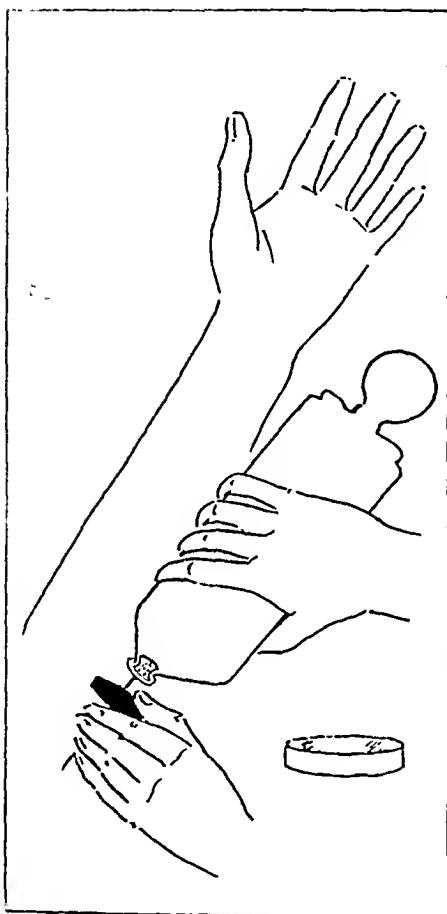


FIG. 8.

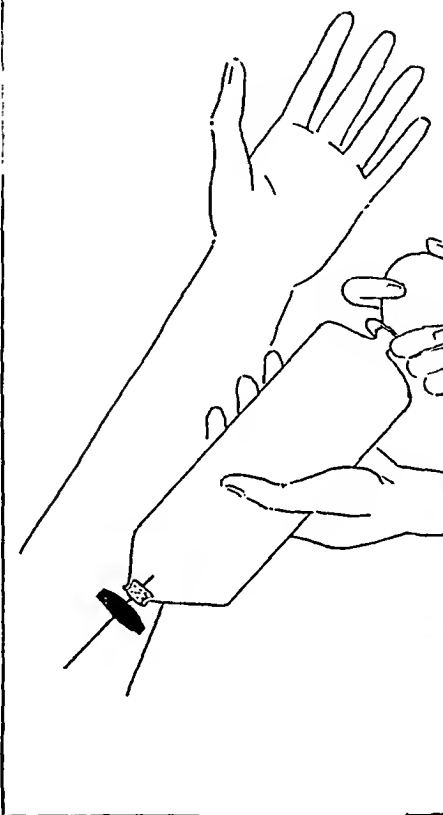


FIG. 9.

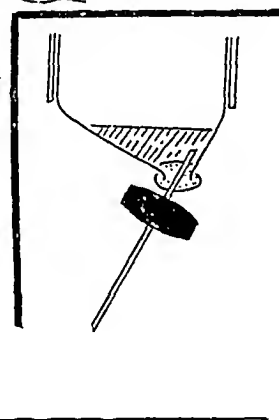


FIG. 10.

FIGS. 8-10.—Remaining steps in the technic of administration of plasma intravenously

of the stylet when the hands of the operator are wet, oily, or bloody. The needle does not clamp on the glass lip extending from bottle B but rides in the rubber stopper allowing some free play, thus, preventing breakage of the glass tip that would occur from motion of the operator's hand transmitted to the rigid needle fixed in the bone.

PROCEDURE FOR INTRAVENOUS ADMINISTRATION OF PLASMA

(1) The large end section of the container is removed and the winged-arms of the protruding bottle are turned clockwise, pushed into the cylinder, then rotated counter clockwise to lock bottle A in place (Fig. 4).

(2) The container is held upright. The rubber bulb D is now pushed home, the metal clip catching over the flange of the upper bottle (Fig. 5).

(3) When all the water has entered bottle B, the container is then agitated for one minute (no less) in order to restore the plasma to a fluid state (Fig. 6).

(4) Remove sterile needle from the top container; insert the needle into vein and then remove the stylet (Fig. 7).

(5) Remove lower cover of container. The rubber stopper of bottle B is now punctured by that portion of the needle extending proximal to the winged arms (Fig. 8).

(6) With the patient lying down, the arm is elevated distally so the container is as near upright as possible, and then by intermittent compression of bulb D the plasma is forced into the vein (Fig. 9).

(7) When the fluid level reaches the red line on the lower bottle, stop compression of the bulb and remove the needle (Fig. 10).

PROCEDURE FOR INTRA-OSSEOUS ADMINISTRATION OF PLASMA

The first three steps are the same as described above.

(4) Remove sterile needle with stylet in place from the container and insert it into the bone (Fig. 11a).

TECHNIC FOR INTRODUCING NEEDLE IN THE MARROW

The site of choice for the injection in patients over five years of age is the manubrium, one centimeter above the angle of Louis, or the body of the sternum, at the third interspace, in the midline. After preliminary local anesthesia with procaine (when possible or necessary), the needle, with its stylet, is inserted vertically with the bevel towards the head of the patient. The periosteum is penetrated gently with a semicircular burrowing motion until a firm hold is obtained. The needle is then tilted, its tip pointed toward the neck of the patient and with the same burrowing motion, the anterior plate of the sternum is penetrated. The needle should not be "jabbed in" or pushed in with force. When the marrow cavity is penetrated, diminution in the resistance to the progress of the needle is felt, amounting sometimes to a trapdoor effect. In the hands of the inexperienced, there is less danger of injury if the needle is inserted in the upper end of the tibia, than in the sternum.

(5) Once the needle is properly fixed in the bone the stylet is removed (Fig. 11b).

(6) The small syringe is then attached and a few drops of bone marrow aspirated, to make sure that the needle is properly placed in the marrow cavity. The syringe is then removed (Fig. 11c).

(7) The rubber stopper of the lower end of bottle B is punctured by that portion of the needle extending proximal to the winged arms (Fig. 12).

(8) By intermittent compression of bulb D, the pressure in the closed system is increased and the plasma is forced through the needle into the marrow and, ultimately into the circulation of the recipient (Fig. 13a).

(9) When the fluid level reaches the red mark on the lower bottle, the

INJECTION UNIT FOR PLASMA

unit is removed (Fig. 13b). The needle is then withdrawn with the same type of semicircular twisting motion used in driving it in.

This plasma injection unit has been tried 20 times in 20 patients, with satisfactory results.

FIG. 12.

FIG. 11 a.

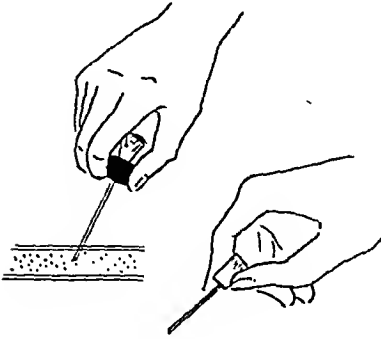


FIG. 11 b.

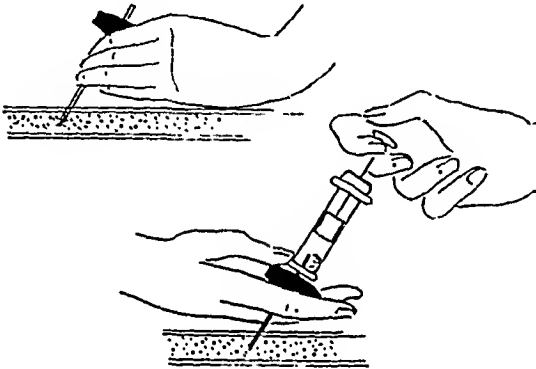


FIG. 11 c.

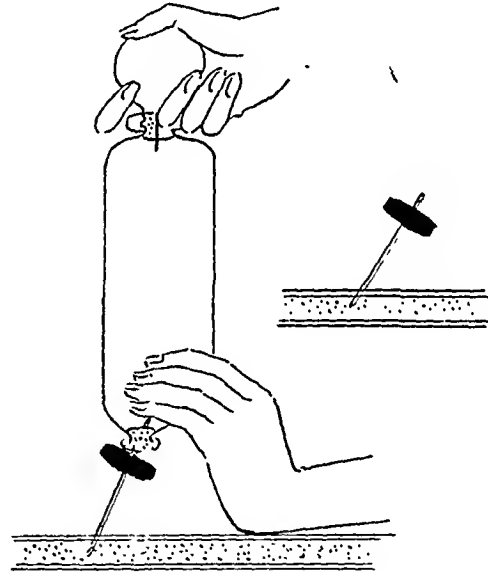
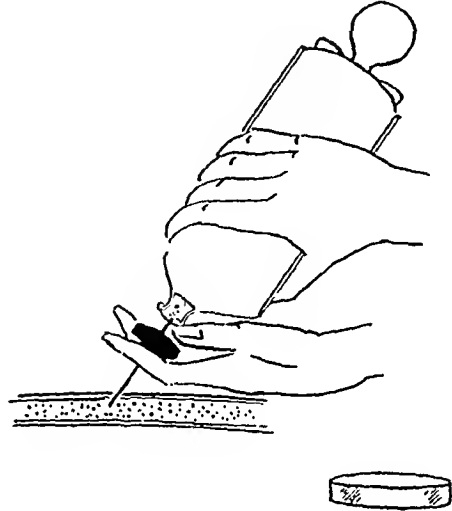
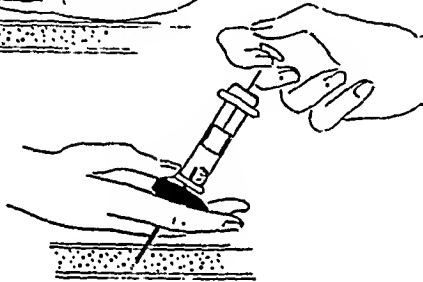


FIG. 13 b.

FIG. 13 a.

FIGS. 11-13.—Steps in the technic of administration of plasma intra-osseously.

The simplicity of the mechanism, light weight, small size, rapid utilization, and choice of two routes of administration, suggest that these units may be used with advantage by mobile groups or isolated personnel, thus, making possible the benefits of plasma to individuals at critical times under adverse conditions.*

* The same unit may be used for the emergency injection of human albumin; the containers holding 200 cc. of 25 per cent albumin solution. It has also been utilized with five grams of the sodium salt of one of the sulfa drugs in the fixed bottle B and 100 cc. of pyrogen-free water in mobile bottle A. When mixed, this results in a five per cent solution of the drug, ready for administration.

The used bottles may be taken apart, sterilized, refilled, and placed back in active service. This salvage will reduce the overall cost of a primarily inexpensive method.

REFERENCES

- ¹ Strumia, M., Newhouser, L. R., Kendrick, D. B., and McGraw, J. J.: Development of Equipment for Administration of Dried Plasma in the Armed Forces. *War Med.* 2, 102-113, January, 1942.
- ² Pitman, L. K.: Simplified Methods for the Administration of Blood Plasma in Emergencies. *J. A. M. A.*, 120, 195-196, September 19, 1942.
- ³ Tocantins, L. M., O'Neill, J. F., and Price, A. H.: Infusions of Blood and Other Fluids *via* the Bone Marrow in Traumatic Shock and Other Forms of Peripheral Circulatory Failure. *ANNALS OF SURGERY*, 114, 1085, December, 1941.
- ⁴ Tocantins, L. M., and O'Neill, J. F.: Infusion of Blood and Other Fluids Into the General Circulation *via* the Bone Marrow. *Surg., Gynec. & Obst.*, 73, 281, September, 1941.
- ⁵ Tocantins, L. M., O'Neill, J. F., and Jones, H. W.: Infusions of Blood and Other Fluids *via* the Bone Marrow: Application in Pediatrics. *J. A. M. A.*, 117, 1220, October 11, 1941.

BOOK REVIEW

BLOOD SUBSTITUTES AND BLOOD TRANSFUSIONS. Edited by Stuart Mudd, M.D., and William Thalheimer, M.D. Charles C. Thomas. Springfield and Baltimore. 1942.

A no more timely and authoritative publication has appeared in surgical literature during this world catastrophe than the monograph on Blood Substitutes and Blood Transfusions by Mudd and Thalheimer. It is a symposium composed of the papers read before the American Human Serum Association at their meeting in 1941.

As the result of the discussion of some seventy contributors at this meeting, an early agreement was reached that the basic etiologic cause of secondary shock was a fall in the circulatory fluid volume of the blood.

Most of the program was largely devoted to such questions as procurement, preservation, administration and the relative efficiency of the various blood substitutes that have been used and recommended, both clinically and experimentally, including human hemoglobin and both human and bovine serum.

Such a group can speak authoritatively on these subjects, and the logical way in which the problem has been arranged results in an invaluable presentation which no active surgeon or hospital library can afford to omit from their shelves.

It is a remarkable contribution and both the writers and the publishers are to be congratulated.

WALTER ESTELL LEE, M.D.

BRIEF COMMUNICATION

IMPROVED TIP FOR MILLER-ABBOTT TUBE

H. B. MORTON, M.D., M.S. (Surg.)
LINCOLN, NEBR.

THE DEVELOPMENT of the Miller-Abbott tube has undoubtedly been one of the greatest advances in the management of intestinal obstruction. A great deal has been written concerning the advantages and limitations of this ingenious device.¹ It is generally conceded that the greatest handicap to the use of this method of decompressing the gastro-intestinal tract is the delay or inability of the tube to traverse the pylorus of the stomach. After the bulb portion of the tube has entered the duodenum its progress down the intestinal tract is usually rapid, and with it a rapid decompression of the small intestine.

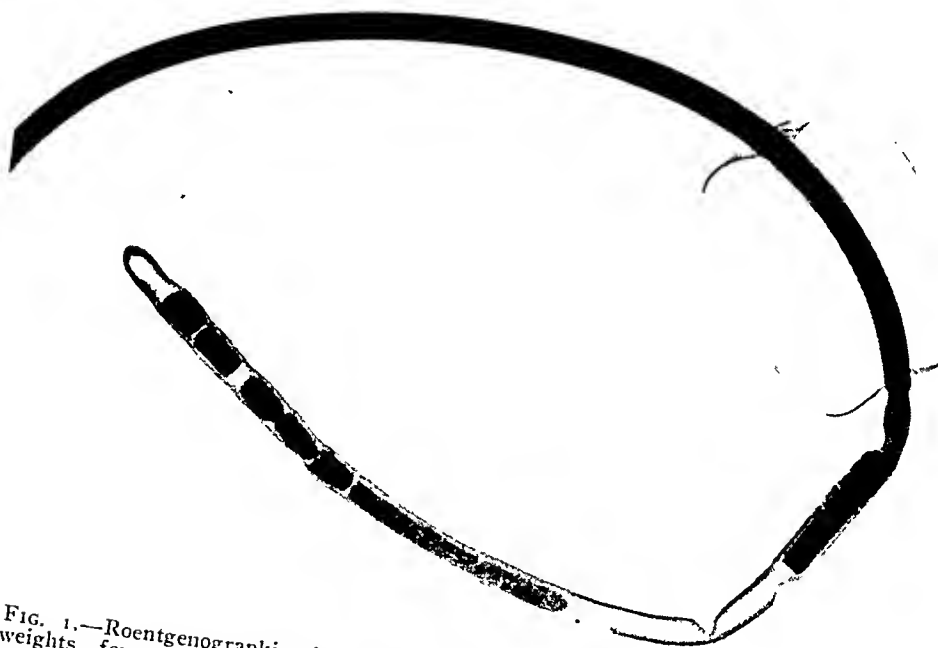


FIG. 1.—Roentgenographic shadow of the special tip to show the arrangement of the weights, fenestra and connector.

This difficulty in getting the Miller-Abbott tube to enter the duodenum is reflected in the development of the Wilson-Sawyer modification,² which consisted in making the tube less flexible. Personal experience with the latter tube proved it to be a definite improvement, but the same difficulty was encountered to a lesser degree.

After experimenting with various modifications of the tip of the tube, one has been found which seems, after repeated trials, a very definite improvement in its ability to enter the duodenum promptly in cases of marked obstruction. On many occasions this tip has entered the duodenum very promptly after prolonged attempts with other tubes have proved futile. My experience with this device is submitted for further trial and evaluation.

The above mentioned special tip employs the element of weight, which is carried by gravity to the outlet of the stomach. This weight also acts to prevent the tip of the tube from coiling back toward the fundus, as often happens with the conventional tube. The weighted tip was made by incorporating lead shots into about five inches of the tip of a Levin tube. This, in turn, was connected by a short metal tube of proper caliber to the cut end of a Miller-Abbott or Wilson-Sawyer tube. Fenestra are incorporated proximal to the weights, but distal to the balloon, so that liquid and gas are removed from the intestine in advance of the tube (Fig. 1).

The technic of passing the tube is essentially that worked out by the originators of the Miller-Abbott tube. It cannot be emphasized too strongly that the successful employment of the Miller-Abbott tube necessitates constant and careful supervision by one willing to give individual attention to it. Personal experience in this respect parallels that described in other excellent articles.³

REFERENCES

- ¹ Abbott, W. O., and Johnston, C. G.: Intubation Studies of the Human Small Intestine. X. A Nonsurgical Method of Treating, Localizing and Diagnosing the Nature of Obstructive Lesions. *Surg., Gynec. and Obst.*, 66, 691-697, April, 1938.
- ² Wilson, D. M.: Intestinal Intubation. I. Studies in Acute and Subacute Obstruction of the Small Intestine. *Proc. Staff Meet. Mayo Clinic*, 13, 666-671, October 19, 1938.
- ³ Blodgett, James B.: A Technic for the Satisfactory Use of the Miller-Abbott Tube. *Am. Jour. of Surg.*, 53, 271-279, August, 1941.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.



THE SURGICAL TREATMENT OF TOPHACEOUS GOUT*

ROBERT R. LINTON, M.D., AND JOHN H. TALBOTT, M.D.

BOSTON, MASS.

FROM THE SURGICAL AND MEDICAL SERVICES OF THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

GOUT is a chronic metabolic disorder associated with an increased concentration of uric acid in the blood. Early in its course it is characterized with few clinical manifestations except acute attacks of arthritis. As the disease progresses osseous and subcutaneous urate deposits appear and lead to physical deformity and persistence of low-grade symptoms. Patients with advanced changes may be seriously handicapped and suffer needlessly, due to the gradual increase in the size of the deposits. Since medicinal measures have been ineffective in treating these disabling tophi⁹ recourse has been made to surgical treatment, with the expectation that considerable benefit would be obtained. The progressive course of the disease in no way has been affected but a lasting local benefit has been achieved that could not be produced by any other measures.

The surgical treatment of tophaceous gout in 11 patients constitutes the basis of this report. The operations were carried out at the Massachusetts General Hospital by the senior author (R. R. L.), or directly under his supervision. This was possible because of the medical study in a large group of gouty patients by the junior author (J. H. T.). In the group of patients treated surgically, there were ten males and one female. The ages ranged from 20 to 80 years. There were two in the third decade of life, one in the fifth, three in the sixth, two in the seventh, two in the eighth, and one in the ninth. Eight, or 73 per cent, were over 50 years of age. Seven patients had had gout for 20 years or more, two for 10 to 20 years, and two for seven years.

Historical Review.—Gout is a disease of great antiquity. Undoubtedly it is as ancient as civilization. Quoting from Garrod¹ (1858): "Gout . . . was probably one of the earliest diseases to which flesh became heir when man began to participate in the luxuries of civilized life: it is a disease, also, which can lay claim to having had among its victims some of the most renowned of the human race from their position, opulence, and intellect." The aphorisms of Hippocrates,² who lived about 350 B.C., indicate that he was well acquainted with the manifestations of gout. Writers on the

* The publication of the colored reproductions was made possible by the contribution of Mr. Arthur E. Lothrop of Brookline, Mass.

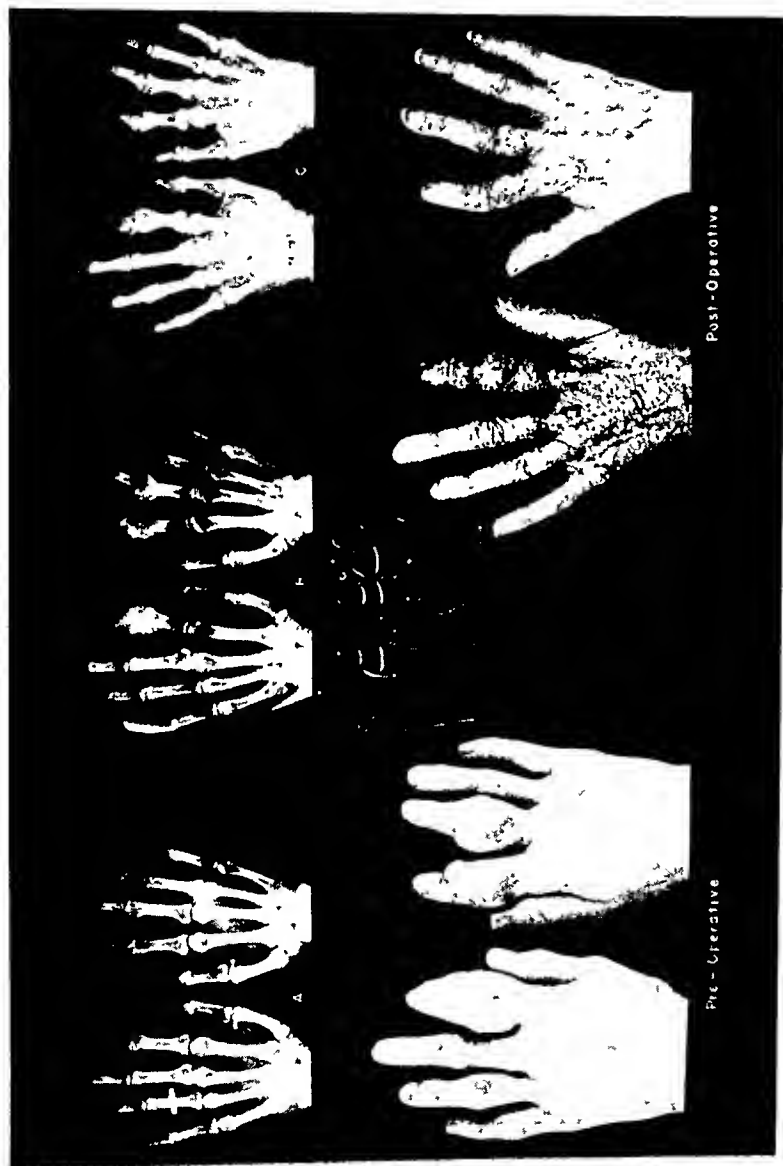


FIG. 1.—Extensive tophaceous deposits of the right and left index fingers and the middle right finger, which involved the phalanges and the extensor and flexor tendons. The patient, a female, age 49, had symptoms of gout for 32 years (The same patient as in Fig. 15). This case illustrates the rapidity with which tophaceous deposits may develop: (A) Roentgenograms, taken in 1933, show only slight evidence of osseous joint destruction. (B) Roentgenograms, taken in 1938, before the operations five years later, show extensive bone and periosteum was preserved as far as possible, which accounts for this new bone formation. The operations were performed under novocain block anesthesia at the base of the fingers. The postoperative photograph and roentgenogram were taken about six weeks after the operations. Some shortening of the fingers, as to be noted and the cosmetic result was not as good as in some of the other cases, although this improved after months, but in view of the extensive involvement of the bones, extensor and flexor tendons, the result was satisfactory, especially since the patient received relief from pain, could again wear gloves, and did not have to hide her hands when in public. Note the transverse incisions which were made, and the excellent healing of them.

subject have been very prolific since that time. Most dissertations, however, have been clinical descriptions, and neither the etiology of the malady nor the pathogenesis of symptoms have been discovered as yet. The most important contribution regarding the treatment of acute gouty arthritis was described first by Alexander, of Tralles, quoting Garrod,¹ in the sixth century. On empiric grounds he recommended the use of hemodactyl, the plant from which colchicum is derived. Among the many interesting volumes on the treatment of gout is one written by Missaurus,⁶ in 1735: "Demonstrating that the Gout is one of the greatest blessings which can befall Mortal Man: That all Gentlemen who weary of it, are their own Enemies; and that those Practitioners who offer it the cure, are the vainest and most mischievous Cheats in Nature."

In contradistinction to the voluminous writings on the medical aspects, little has been written on the surgical treatment. In 1641, Paré⁷ opened painful areas about tophaceous joints with the cautery and rubbed them with hemodactyl, gentian, mercury, or alum. Hippocrates² resorted to actual burning of the painful areas. He says in his "Treatise of Diseases," speaking of gout: "The Disease is indeed long and grievous, but not mortal; but if the Pain remains in the toes, burn them above the joints with Crude Flax." This method, according to Hutchinson,³ was revived in the seventeenth century by Hermon Busschof, a Minister at Batavia, in the services of the Dutch East India Company. The method described by Busschof consisted in placing a small piece of Indian moss over the painful tophus and then setting fire to it. This treatment apparently afforded relief, since Busschof, a victim of the malady, admitted extraordinary alleviation of pain. Another patient, Sir William Temple, reported: "That when the Pain in his Great Toe was very violent, and he, in five Days, had not been able to stir his foot, but as it was lifted, he was suddenly relieved by the Moxa (burning of it), and walked half a dozen turns about the Room without pain or Trouble to the Surprise of those that were about him, as well as his own."

Hutchinson,³ in 1880, was the first to report the surgical removal of two toes on account of suppuration of tophaceous deposits. Riedel,⁸ in 1904, stated that the removal of urate deposits could be accomplished if the gouty arthritis were localized to the metatarsophalangeal joint of the great toe. He performed two operations, one on a man, age 45, and the other on a woman, age 70. A preoperative diagnosis of suppurative arthritis was made in each instance, and not until he discovered urate crystals in the bursae and the synovial membranes at the time of operation did he appreciate that the patients were suffering from an acute attack of gout. In each case he simply opened the joint space and removed as much of the urate crystals as possible, then left the wound open to heal by secondary intention. The incisions healed in a few weeks, following which one patient was free of attacks for 14 years and the other for eight years, or until her death.

Lindsay,⁴ in 1913, found that healing occurred naturally, provided the incision was made over the more healthy skin towards the base of the



Pre- Operative

Post- Operative

FIG. 2.—Tophaceous deposits involving the index and fourth fingers of the right hand. The patient, a male, age 69, had symptoms of gout for 15 years (The same patient as in Fig. 9). The roentgenogram shows moderate involvement of the bones. Only the tophus on the fourth finger was removed, at the patient's request, but since he obtained such a satisfactory result on this one he is planning to have the one on the index finger removed. The operation was performed under novocain block anesthesia at the base of the finger. The tophus was removed through a transverse incision. It involved the extensor tendon but it was possible to preserve a portion of it so it was only necessary to splint the finger until the wound healed. The interphalangeal joint capsule and the cartilages were involved. The patient was pleased with the cosmetic result, volunteering the information that he no longer tried to hide his hand while in public. The photographs show the hand before operation and four months later.

tophaceous swelling. Thomson, quoted by Llewellyn,⁵ in 1920, reported two cases in which gouty deposits contiguous to tendon sheaths, bursae and skin were removed. The deposits in one man, age 30, had involved the extensor tendons over the fingers, and in the other, a man, age 37, large tophi were located about the left external malleolus, the left olecranon and the right malleolus. All were subcutaneous except the one about the left malleolus, where bone, ligaments, and peronei tendons were involved. The patients did well following the operations and no further gross tophaceous deposits developed.

A survey was made of the records at the Massachusetts General Hospital from 1835 to 1935, in order to determine how many patients with gout had been operated upon for the treatment of tophaceous deposits. Only seven cases could be found. The operative procedure consisted of evacuating the tophi in three patients, while amputations were carried out on four. The earliest operation was performed in 1878, by Dr. J. C. Warren. It seems difficult to understand why surgery was not performed more frequently in the treatment of deformed tophaceous joints and tophaceous deposits. Perhaps it was because an acute attack of gouty arthritis, with its classical insignia of "tumor, rubor, color, *et dolor*" was so frequently mistaken for an acute infection, and it still is by those not acquainted with the vagaries of gout. Furthermore, it was not realized that considerable relief of symptoms and rehabilitation of the patient could be obtained by surgery.

Diagnosis.—The diagnosis of gout in the tophaceous stage of the disease is not difficult.¹⁰ A history of acute attacks of arthritis with complete relief from symptoms between attacks is usually obtained. If subcutaneous deposits of urate crystals have developed, roentgenograms of the extremities usually will show evidence of bony involvement. The characteristic roentgenologic appearance of a gouty joint includes "punched-out" areas, soft tissue swelling, diminution of joint space, and sometimes extensive destruction of the joint with ankylosis (Figs. 1, 6, 8 and 9). The concentration of uric acid in the blood serum (in contrast to whole blood) is above 6.0 mg. per 100 cc. The serum uric acid is increased between attacks as well as during attacks, and should always be determined in a suspected case of gout. If a sinus has formed in a subcutaneous tophus, the chalky exudate will reveal urate crystals on microscopic examination. A final confirmatory diagnostic procedure is the favorable response to full doses of colchicine if given during an acute attack.

The differential diagnosis between an acute attack of gouty arthritis and joint sepsis warrants *especial consideration*. Undoubtedly, many acute gouty joints have been operated upon because the surgeon considered the condition one of sepsis. This is not surprising, since there may be general as well as local manifestations of a severe infection in acute gout. These include fever, a leukocytosis of 15,000 to 20,000, and prostration. The absence of an ascending lymphangitis from the acutely inflamed gouty joint is a helpful differentiating sign. Fulminating sepsis involving a tophaceous



FIG. 3.—A large tophaceous deposit with a small draining sinus involving the dorsum of the hand. The patient, a male, age 80, had symptoms of gout for seven years. The operation was performed under ether anesthesia. The extensor tendons of the second, third and fourth fingers had to be excised with the tophus because they had been so infiltrated with urate crystals that they were unrecognizable. Despite this, a good functioning hand was obtained by splinting the fingers in extension for eight weeks, then commencing gentle massage and active motion. The drawing shows the incision. A portion of the skin sloughed because of the extensive dissection. This necessitated a secondary skin graft. The photographs show the hand before operation and two and one-half years later, with no evidence of recurrence.

FIG. 4.—A large tophaceous deposit involving the proximal interphalangeal joint of the fifth finger of the right hand and the extensor tendon of it. The patient, a male, age 59, had symptoms of gout for 36 years. The tophus was removed through a transverse incision under novocain block anesthesia at the base of the finger. There was destruction of the proximal end of the middle phalanx and the distal end of the proximal phalanx, with some shortening of the digit which is a little more marked in the postoperative view. The photographs show the hand before operation and one year later, with no evidence of recurrence.

joint is an extremely rare condition, so that immediate surgery in acute gout rarely ever is indicated. Tophaceous deposits about a joint not infrequently rupture through the skin and discharge urate crystals. This may leave an ulcerating lesion (Figs. 3, 5, 6, 7, 8 and 9). Cultures taken from these lesions, in our experience, have shown only the usual bacterial flora found on the normal skin, and in no instances has it been necessary to incise and drain such a lesion. The differentiation between acute gout and sepsis, therefore, should not rest on the local signs and systemic findings but upon a careful evaluation of all of the medical data. An accurate history, with particular reference to previous attacks of joint symptoms, is of utmost importance. An examination of the patient for evidence of tophi elsewhere on the body may give the true diagnosis. Roentgenologic examination of the affected part, and estimations of the blood serum uric acid level in doubtful cases are important diagnostic aids.

Indications for Surgery.—The surgical treatment of gout is applicable only to patients who have developed large tophaceous deposits. Less than ten per cent of all gouty patients studied by the junior author have needed surgical treatment. In the group of patients reported, surgery was limited to the removal of urate deposits which involved the bony and soft structures about the elbows, forearms, wrists, hands, and feet. Elsewhere in the body, especially about the knee joints where very large tophi appear, removal was not found necessary, but if the occasion should arise they could be similarly treated. The indications for surgical treatment are believed to be: (1) Cosmetic reasons when tophi have become large and unsightly, such as in the subcutaneous tissues of the fingers, the dorsum of the hand, forearm, or wrist (Figs. 1, 2, 3, 4 and 5). In this category may be included smaller tophi on the hands and feet which interfere with the wearing of gloves and shoes. (2) Pain in tophi because of their location over exposed areas of the body, such as those involving the olecranon bursae, knuckles, terminal ends of the fingers, toes and heels (Figs. 2, 4, 6, 8, 9 and 16). (3) Interference with the movements of tendons or adjacent joints by tophi that involve the extensor or flexor tendons of the hand (Figs. 5 and 11). (4) Any discharging sinus associated with a tophaceous deposit (Figs. 3, 5, 6, 7, 8, 9 and 16). (5) Extensive phalangeal involvement of the fingers or toes with urate deposits (Figs. 1 and 9).

Surgical Pathology.—The tophaceous deposits which were removed during this study may be divided into three anatomic types: (1) bursae and subcutaneous deposits which have involved only the tissues superficial to the deep fascia; (2) deposits which arise in tendons and which may or may not have involved adjacent tissues, such as fat, fascia, bursae, and skin; and (3) deposits which arise in joints with involvement of the bones, tendons, bursae, subcutaneous tissues, and skin.

All of the tophi involving the soft tissues had a definite fibrous capsule, which was thin and transparent but tough (Figs. 11, 12, 15 and 16). It is thought to be formed from connective tissue and is, therefore, not a

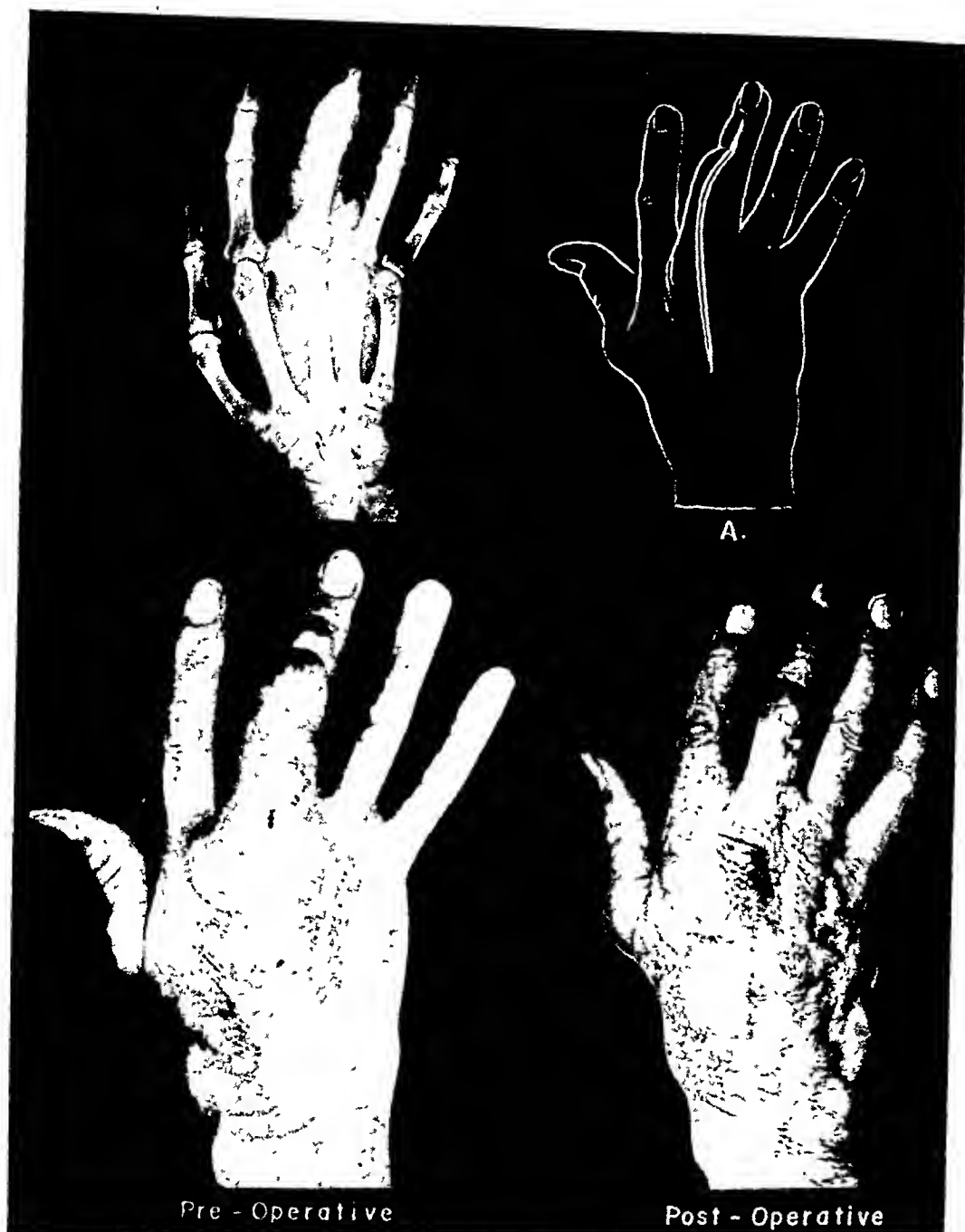


FIG. 5.—A large tophaceous deposit, with draining sinuses on the dorsum of the right hand. The patient, a male, age 65, had symptoms of gout for 20 years (The same patient as in Fig. 8). The roentgenogram shows ankylosis of the proximal interphalangeal joint, with little bone destruction. The operation was performed under ether anesthesia. The extensor tendon was so infiltrated with urate crystals that it was necessary to remove it from the base of the metacarpal bone to the base of the terminal phalanx. Despite this, excellent function was restored by splinting the finger in extension for eight weeks, then commencing gentle massage and active motion. This was one of the earliest cases operated upon using a longitudinal incision as shown in the drawing, which resulted in marked sloughing of the skin flaps necessitating a secondary skin graft. Multiple transverse incisions would have obviated this complication. The photographs show the hand before operation and two years later, with no evidence of recurrence.

true capsule. The formation of it is considered to take place with the deposition of urate crystals in the tissues. As the tophus gradually increases in size it replaces the subcutaneous fat and forces aside the fibrous connective tissue, thus forming a capsule. Some of the fibrous tissue may be infiltrated with urate crystals instead of being forced aside since on the cross-section of a tophus a stroma of interlacing fibers may be seen dividing it into numerous lobules (Fig. 12). The lobulated appearance is evident on the surface of all cleanly dissected tophi in which the capsule is intact (Figs. 11, 12, 15 and 16). The urate crystals rarely infiltrate through the subcutaneous tissues. When this occurred it was thought to have followed rupture of the capsule due to trauma or an acute attack of gout, when the contents of the tophus may be partially fluid and under considerable tension. When bones or tendons were involved a capsule was not encountered unless the urate crystals had pushed out into the soft tissues surrounding these structures. It is of interest to note that the urate crystals did not invade blood vessels or nerves, although they often surrounded them. Tendons, on the other hand, were very frequently infiltrated with urate crystals and in some instances so complete was the replacement with urate crystals that no tendinous structure could be recognized.

Tophaceous deposits of long standing were found to be very dry and chalk-like on cross-section (Fig. 12). If there had been a recent attack of acute gout, the urate crystals were suspended in a fluid which gave the appearance of pus. It is believed that the pain in a tophaceous deposit associated with an acute attack of gout may result from the tension produced by the rapid deposition of urate crystals in a semifluid state within the relatively nonyielding fibrous capsule of the tophus. Evidence in favor of this theory is the fact that when a tophus was decompressed by partial excision of the capsule and evacuation of the contents the patient was relieved of pain even though the urate crystals were not completely removed. The relief of pain following the spontaneous rupture of a tophus adds support to this theory.

Analysis of Operations.—The operations were carried out over a seven-year period, 1935 to 1941, inclusive. Forty-six operative procedures were undertaken on 11 patients. Several tophaceous deposits were removed at one operation in many instances. The number of operations per patient varied from one to ten. Six patients had five or more, three had one, one had three, and another two. The operations were divided equally between the hands and feet. There were 41 operations on the feet and toes, 40 on the hands and nine on the forearms and elbows. Local anesthesia, with one per cent novocain solution, was employed in 24, ether in nine, spinal anesthesia in 12, and no anesthesia in one.

An analysis of the lesions shows that there were 31 subcutaneous tophi, 36 involving tendons and adjacent structures, and 26 which arose from joints with bone and soft tissue invasion. Further analysis of the statistics shows that in the subcutaneous group there were eight on the fingers, most fre-

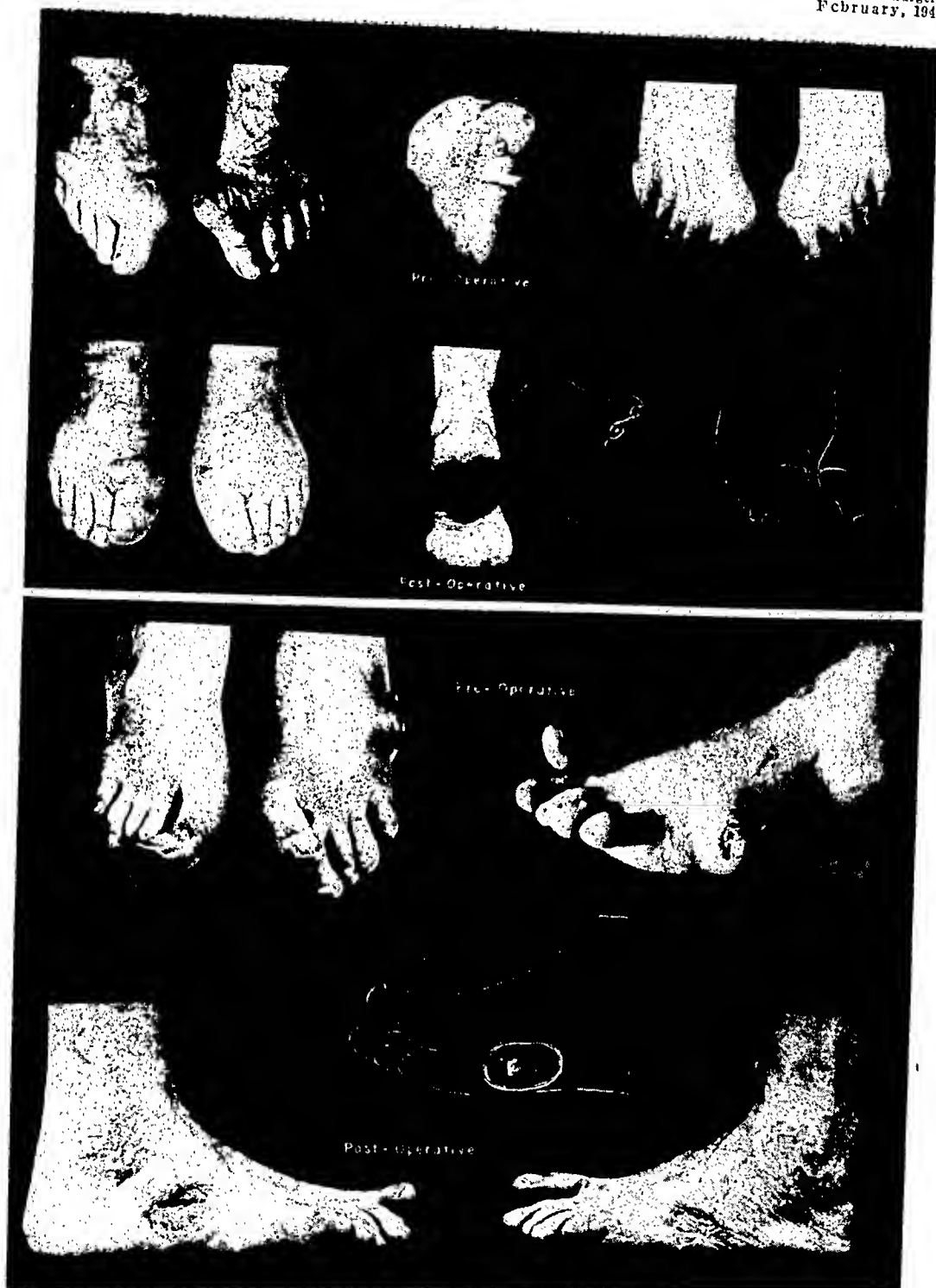


FIG. 6.—Tophaceous deposits involving the first metatarsophalangeal joints of both feet and the left heel. The patient, a male, age 55, had symptoms of gout for 26 years (The same patient as in Figs. 10 and 16). The operation was performed under spinal anesthesia. Note the draining sinuses in the tophus of the heel. Roentgenograms of the feet show some destruction of the proximal phalanges and the first metatarsal bones, but most of the articular surfaces were intact, so that the great toes were not amputated. The drawing shows the incisions employed. The photographs show the lesions before surgery and the left foot two years and the right foot and left heel one year later, with no evidence of recurrence.

FIG. 7.—Tophaceous deposits on the lateral side of the feet. On the right foot the skin was intact but on the left there was a large ulceration with urate crystals visible in the center. The patient, a male, age 70, had symptoms of gout for 30 years. The tophi involved the peronei tendons at their insertions into the tarsus. The operations were performed under spinal anesthesia. The deposits were excised with the overlying skin (see drawing). The tendinous structures were preserved by curettage of the urate crystals. Thiersch skin grafts were applied to the denuded areas, resulting in well healed wounds. The patient thereafter was able to wear his regular type of shoe without discomfort. The photographs show the feet before operation and two years later, with no evidence of recurrence.

quently on the flexor surface, three on the forearms, four involving the olecranon bursae, seven on the toes, eight on the heels, and one on the lateral side of the foot. There were 13 extensor tendons of the fingers and thumbs operated upon, 12 extensors of the toes, four extensors on the dorsum of the hands, two flexors of the fingers, one flexor in the palm of the hand, two triceps tendons, one tibialis anticus tendon, and two involving the peronei tendons at their insertion on the tarsus. The cases with joint, bone and soft tissue involvement included 12 fingers, some with metacarpal involvement, 14 toes, six of which had involvement of the metatarsophalangeal joints, five being of the great toe, the typical location for gout to manifest itself. It is of interest to note that of the 93 tophaceous deposits operated upon only approximately five per cent occurred at this latter site.

Operative Technic.—The successful operative results are attributed to meticulous surgical technic and the adherence to certain rules that evolved during the study. The incidence of arteriosclerosis among gouty patients both young and old is an important factor to be considered. Great care must be taken to maintain an adequate blood supply, particularly in the lower extremities. Incisions should be made so that when closed they will not be subjected to unnecessary tension lest sloughing of the skin occurs. Arterial tourniquets were employed on the finger operations, using a rubber band at the base, but they are contraindicated for operations carried out on the feet because they may damage an arteriosclerotic artery sufficiently to produce arterial thrombosis, with resulting gangrene of the foot. The carrying out of surgery by the most atraumatic method possible cannot be overemphasized.

A tophaceous deposit may be removed by one of two methods. Complete excision of the tophus with its surrounding capsule is preferable. This procedure was followed for all of the large tophi in the soft tissues, such as the olecranon bursa (Fig. 16), subcutaneous tissues of the forearm, hand, and foot where tendons were not involved. Curettage with a small bone curette was the second method. This procedure was used for the removal of the small subcutaneous tophi after making an incision through the overlying skin. If the tophaceous deposit involved the bones or tendinous structures, such as the triceps tendon or a flexor tendon, the major part of the tophus was excised and the remainder was removed by curettage in order not to destroy important structures (Figs. 11, 15 and 16).

The surgical procedures on the hands were, of necessity, more conservative than those on the feet. It is important to preserve the fingers in spite of extensive urate infiltration (Fig. 1). One badly involved finger was amputated early in the study, but as more cases were encountered it was found unnecessary to sacrifice these digits despite extensive urate deposits in the tendons and phalanges, since removal of the tophi resulted in relief of pain, improved cosmetic appearance and partial rehabilitation. The periosteum and bony shell of a phalanx was preserved insofar as was possible. The situation in many cases appeared hopeless when judged roentgenologically (Fig. 1), but a significant quantity of bony shell and periosteum

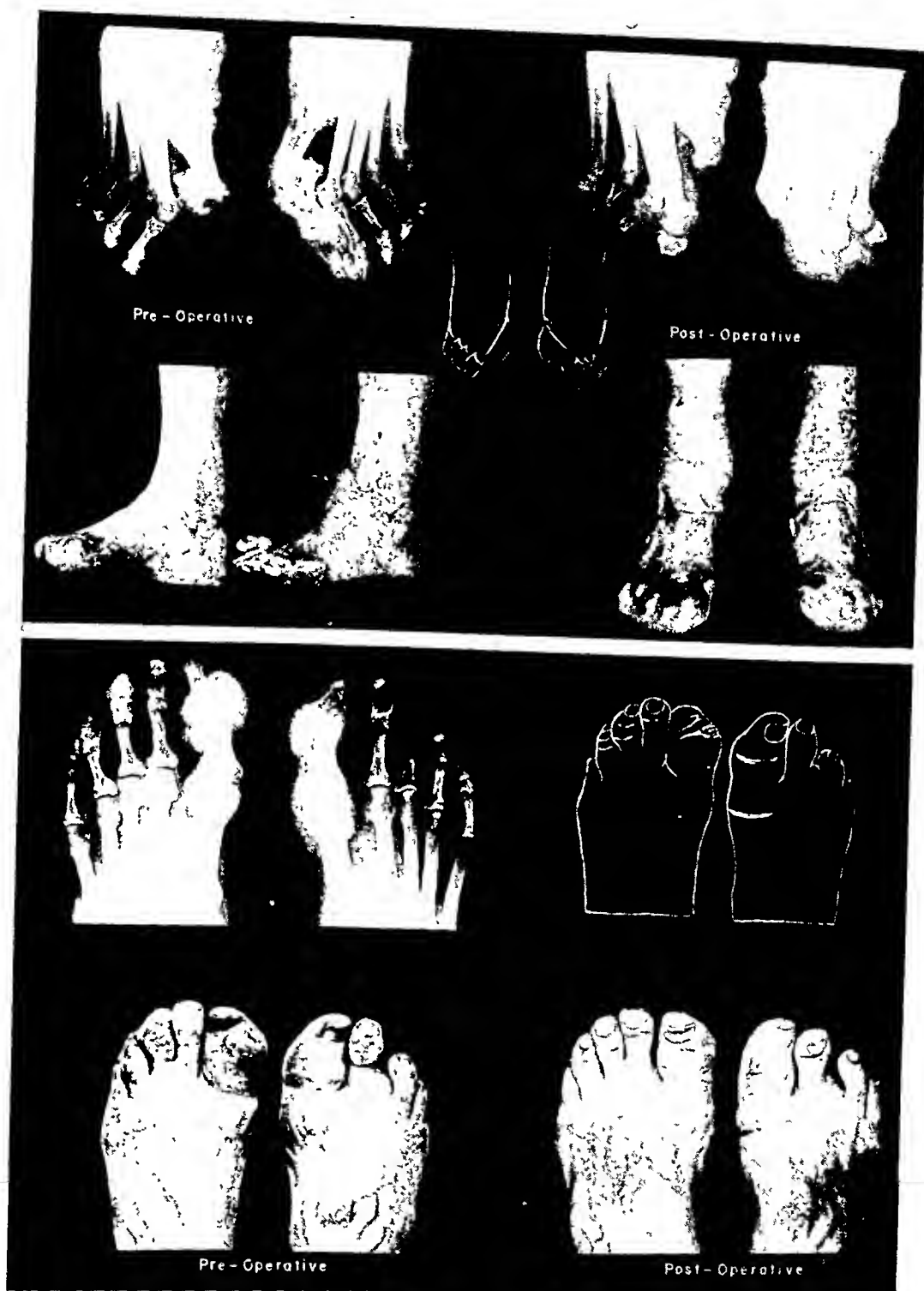


FIG. 8.—Extensive tophaceous deposits of all toes with marked involvement of the metatarsophalangeal joints of the great toes, the terminal phalanges of the other toes, and one in the tibialis anticus tendon of the left foot (marked by an arrow). The patient, a male, age 65, had symptoms of gout for 20 years (The same patient as in Fig. 5). The right great toe had been amputated several years previously at another hospital, but the wound had never healed because the removal of the disease was not sufficiently radical. The draining sinus is seen in the preoperative photograph. The operations were performed under ether anesthesia. The head of the right first metatarsal, the left great toe and the head of the first metatarsal, and the left fifth toe and the head of the fifth metatarsal were amputated through raequet-type incisions. The remaining toes were amputated through the base of the proximal phalanges using lateral skin flaps. This patient and one other were the only ones upon whom such radical surgery was carried out. Both patients obtained excellent results, as they were able to walk without pain. They used the specially constructed type of shoe shown in Figure 13, which permitted them to walk with a normal gait. The photographs show the feet before operation and two years later, with no evidence of recurrence.

would be found at operation. If this could be saved a useful finger was obtained despite the fact that the interphalangeal joints were destroyed.

Removal of the tophaceous deposits involving the toes without amputation also is recommended if roentgenologic examination reveals any of the joint surfaces of the phalanges or metatarsals to be intact (Figs. 6 and 9). When there was marked destruction of these bones (Fig. 8) the treatment of choice was amputation through the proximal phalanx, using lateral skin flaps. If the first or fifth toes were amputated the head of the metatarsal was removed with it, using a racquet-type of incision (Fig. 8). The end-results justified these procedures, since the patients were able to walk in comfort and with practically a normal gait, instead of being limited to a wheel-chair existence. All the toes were removed in a few patients, and despite such radical surgery the rehabilitation of the patient was very gratifying. A specially constructed shoe was developed for these patients which had a forked shank of steel incorporated in the layers of the sole (Fig. 13). The shank is almost as long as the foot before amputation of the toes. This type of shoe allows a spring to the patient's gait which otherwise would be lacking.

If a tophaceous deposit involved an important tendon, such as a flexor tendon of a finger (Fig. 11), the tibialis anticus (Fig. 8), or a triceps tendon (Fig. 16), it was deemed important to remove the tophus leaving as much as possible of the tendon. When the extensor tendons of the fingers were involved, either over the digits themselves or the dorsum of the hand, it was impossible to recognize the tendons in many cases so that the remnants of them had to be sacrificed. Despite this, with careful postoperative splinting and rehabilitation, the majority recovered the use and function of fingers and hands. The extensor tendons of the second, third, and fourth fingers on the dorsum of the hand were removed in one patient. Nevertheless, he obtained a very serviceable hand (Fig. 3).

Every precaution was taken to prevent trauma to the parchment-thin skin which overlies many tophi. Sharp scalpel dissection was used to dissect it from the tophaceous deposit. The skin was retracted by means of sutures in the skin edges and as the dissection was carried toward the base of the tophus fine rake retractors were used. The incision was closed with vertical mattress sutures of silk to prevent infolding of the edges. A plaster splint was applied for immobilization whenever a tendon or a joint was involved. The first dressings were usually done in ten days to two weeks. The skin sutures were removed at that time.

FIG. 9.—Tophaceous deposits involving the toes. The patient, a male, age 69, had symptoms of gout for 15 years (The same patient as in Fig. 2). The third toe on the right foot had been amputated two years previously by another surgeon because of a painful tophaceous deposit involving it. The roentgenograms show marked destruction of the terminal phalanges in the left and right first and second toes and the left third and fourth toes. There was also a large tophus involving the right metatarsophalangeal joint. The skin was ulcerated over the tophus on the left great toe, which had necessitated daily dressings for many months. The urate crystals can be seen in the base of the ulceration and through the parchment-thin skin over the other tophi. Through transverse incisions, as demonstrated in the drawing, all these deposits were removed under spinal anesthesia at one operation. The wounds healed *per primam*. Amputation of the toes was not considered necessary because the tophi were chiefly in the distal ends of the digits and the metatarsophalangeal joints were relatively uninvolved. The photographs show the feet before operation and four months later.

The types of incisions which were used are of extreme importance, especially on the fingers and toes. The first operation for the removal of a tophaceous deposit on a finger was undertaken through lateral incisions, one on either side of the finger. This gave an adequate exposure and it was possible to remove the urate crystals without difficulty. The skin between the two incisions sloughed, unfortunately, and the wound healed by secondary

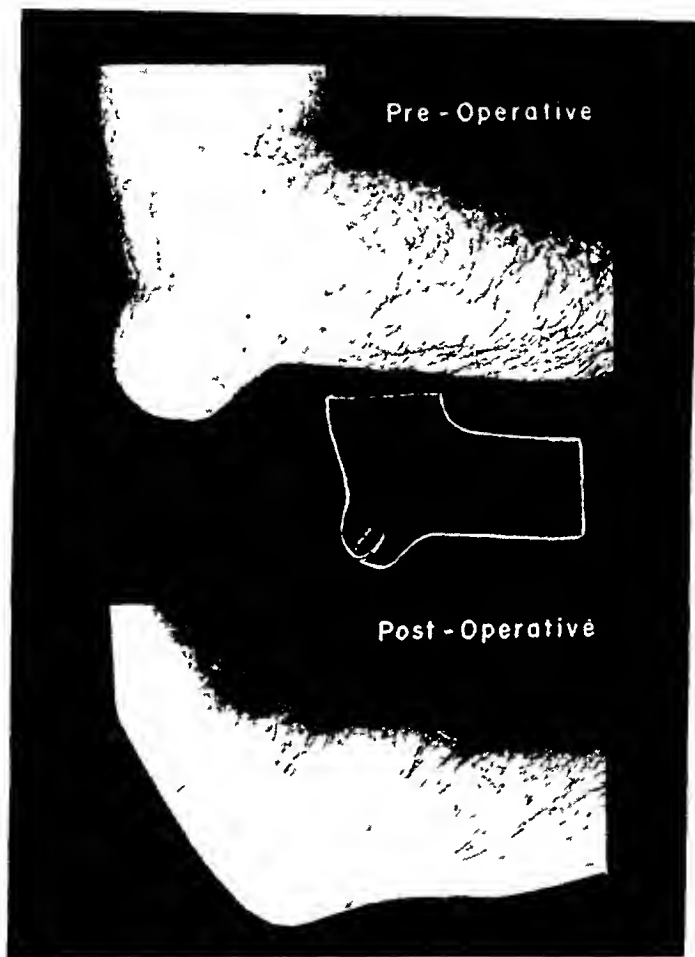


FIG. 10.—A large tophus of the elbow involving the olecranon bursa and the insertion of the triceps tendon. The patient, a male, age 55, had symptoms of gout for 26 years (The same patient as in Figs. 6 and 16). The operation was performed under ether anesthesia. The urate crystals were curetted from the tendon in order to preserve the attachment of this important structure. The drawing shows the incision. The photographs show the elbow before operation and one year later, with no evidence of recurrence.

intention. Early in the series another large tophaceous deposit, which extended from the base of the third metacarpal to the base of the terminal phalanx on the dorsum of the hand (Fig. 5), was removed through a long incision extending over the entire length of the tophus. It was necessary to remove the extensor tendon with the tophaceous deposit because it had been practically destroyed by infiltration with urate crystals. Once again, the skin edges of the wound sloughed and it was necessary to do a secondary

SURGERY OF TOPHACEOUS GOUT

skin graft in order to heal the wound. A satisfactory result was obtained but it required several additional weeks (Fig. 5).

Following this incident all tophaceous deposits on the fingers, hands, toes and feet were removed through single or multiple transverse incisions. Care was taken to avoid severing the digital arteries. Sloughing of the skin edges was never a factor after this type of incision was adopted. Similar

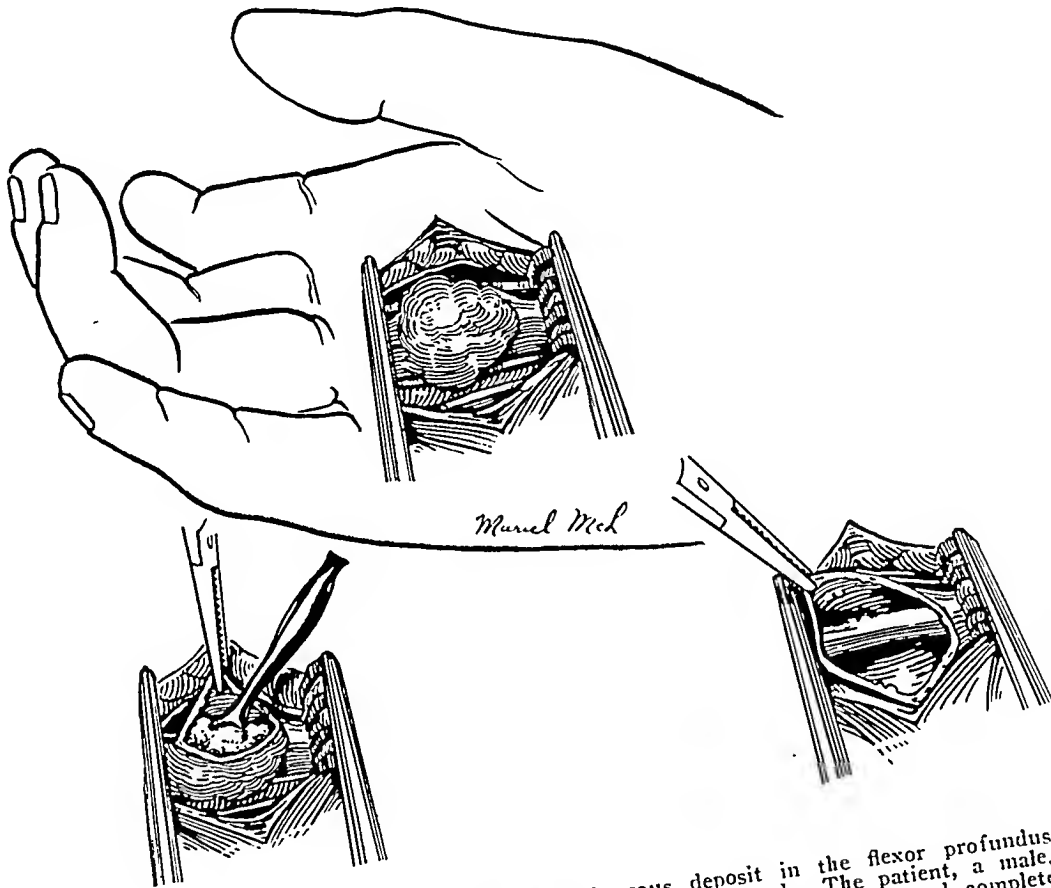


FIG. 11.—A drawing showing a tophaceous deposit in the flexor profundus tendon of the left fourth finger in the palm of the hand. The patient, a male, age 28, had symptoms of gout for seven years. The tophus prevented complete extension of the finger. The operation was performed under local anesthesia, through a transverse incision. The tophus was limited to the tendon. It was lobulated and covered with a thin capsule. The removal was accomplished mainly with a curette in order to avoid excising too much of the tendon. Since so much of the tendon was involved complete removal was impossible for fear the tendon would rupture. As a result, the tophus recurred and a second operation was performed two years later, at which time a more radical removal was attempted. Again, three years later there is only slight evidence of recurrence but no interference with flexion of the finger. The patient is one of the youngest in the group and has the most marked and disabling tophaceous deposits involving practically all of his joints.

transverse incisions in the cleavage planes of the skin were used for the removal of the olecranon bursae or tophaceous deposits in the forearms, wrists and heels. It was found most satisfactory to incise the skin directly over the tophaceous deposits (Figs. 15 and 16) rather than to make the incision at the base of them in sound skin, as advised by Lindsay.⁴

The treatment of ulcerating tophaceous deposits which involved the first or fifth metatarsophalangeal joint of the foot was most satisfactory by amputation of the toe through the body of the metatarsal bone. The in-

cision was a racquet-type which extended around the base of the toe and up along the inner or outer side of the foot in order to expose the metatarsal bone (Fig. 8). It was possible to circumvent any ulcerated lesion on the side of the joint with this type of incision and when closure was made there was adequate skin to close the wound without tension. The metatarsal was divided either at the middle or junction of the middle and distal thirds in most instances (Fig. 8). This was necessary usually because of extensive involvement of the marrow cavity with urate crystals. The sesamoid bones were always removed when this procedure was carried out. If the remaining toes were involved, these were usually amputated through the proximal phalanx, leaving only a small portion of the base (Fig. 8). Lateral skin flaps were used because the blood supply to these is more adequate than

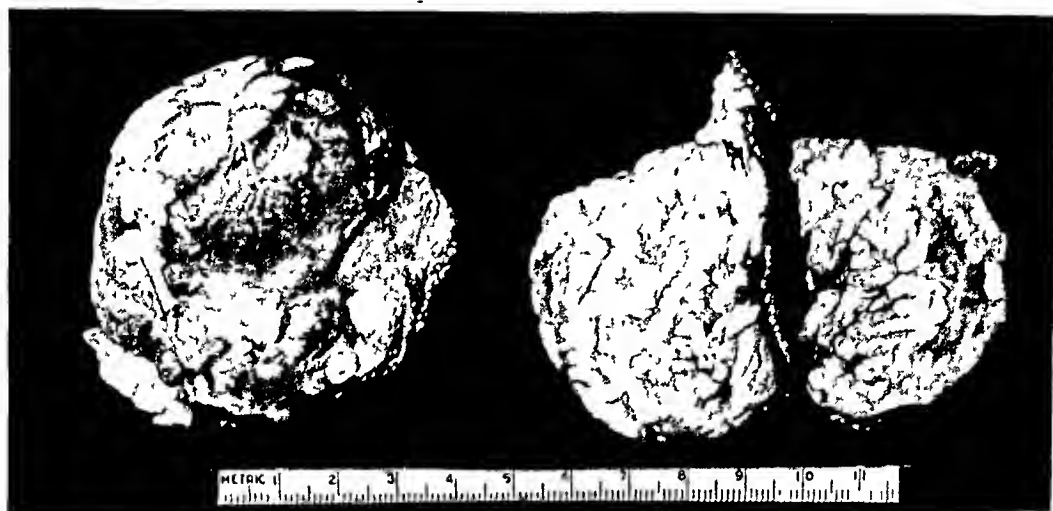


FIG. 12.—A large tophaceous deposit excised from the subcutaneous tissues of the heel. The patient, a male, age 55, had symptoms of gout 26 years (The same patient as in Figs. 6, 10 and 16). A. Note the lobulated appearance of the tophus which is covered with a thin transparent capsule. B. The cross-section of the tophus shows the chalk-like appearance and the stroma of interlacing fibers of connective tissue dividing it up into numerous lobules.

the anterior or posterior flaps. The involvement of the first metatarsophalangeal joint with destruction of the proximal phalanx and the first metatarsal bone was less extensive in some of the cases. When there was no ulceration of the overlying skin the tophus was exposed through a transverse incision (Fig. 16). The greater part of it was cut away with a scalpel and the remainder removed by curettage. It was possible by this means to remove practically all of the tophaceous deposit without sacrificing the great toe although it had destroyed the major part of the joint and completely surrounded it pushing aside tendons, nerves and blood vessels. The results obtained in these cases were very gratifying (Figs. 6 and 9).

A large residual cavity was unavoidable following the removal of a tophaceous deposit that had destroyed a joint. This always filled with blood (Fig. 15) which either organized eventually to form a fibrous union between the bones, or ossified and ankylosed. If the bony destruction was

marked there was considerable shortening of the digit after healing (Figs. 1 and 4). Postoperative drainage was unnecessary and even is considered contraindicated in these cases.

Ulcerating tophaceous lesions were encountered on the lateral side of the foot in some patients (Fig. 7). The method of handling this type of lesion was different than the others. Since it was impossible to remove the tophus without interfering with the blood supply of the overlying skin this was excised with the tophaceous deposit. The urate crystals in such cases had usually invaded the tendinous structures of the foot so that it was necessary to complete the removal by curettage. A large raw surface several centimeters in diameter remained which would have taken many weeks to epithelialize. Healing was hastened by suturing a Thiersch skin graft over the raw surface. A very satisfactory "take" followed each instance this was

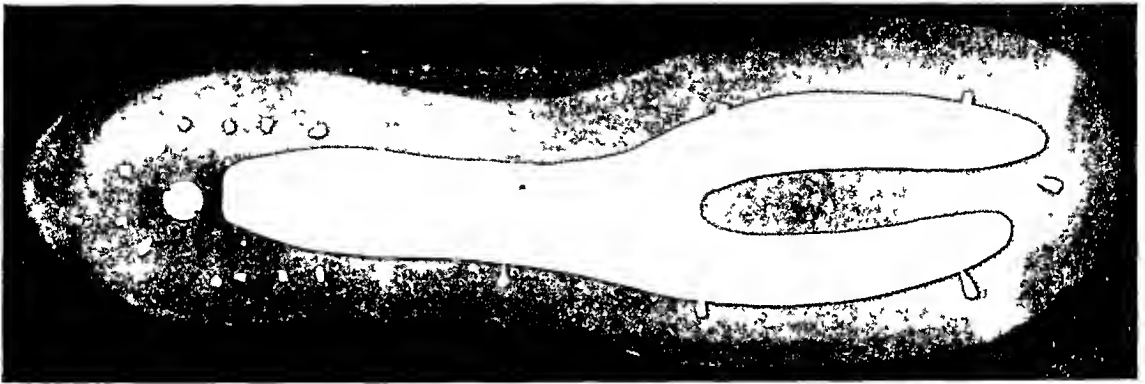
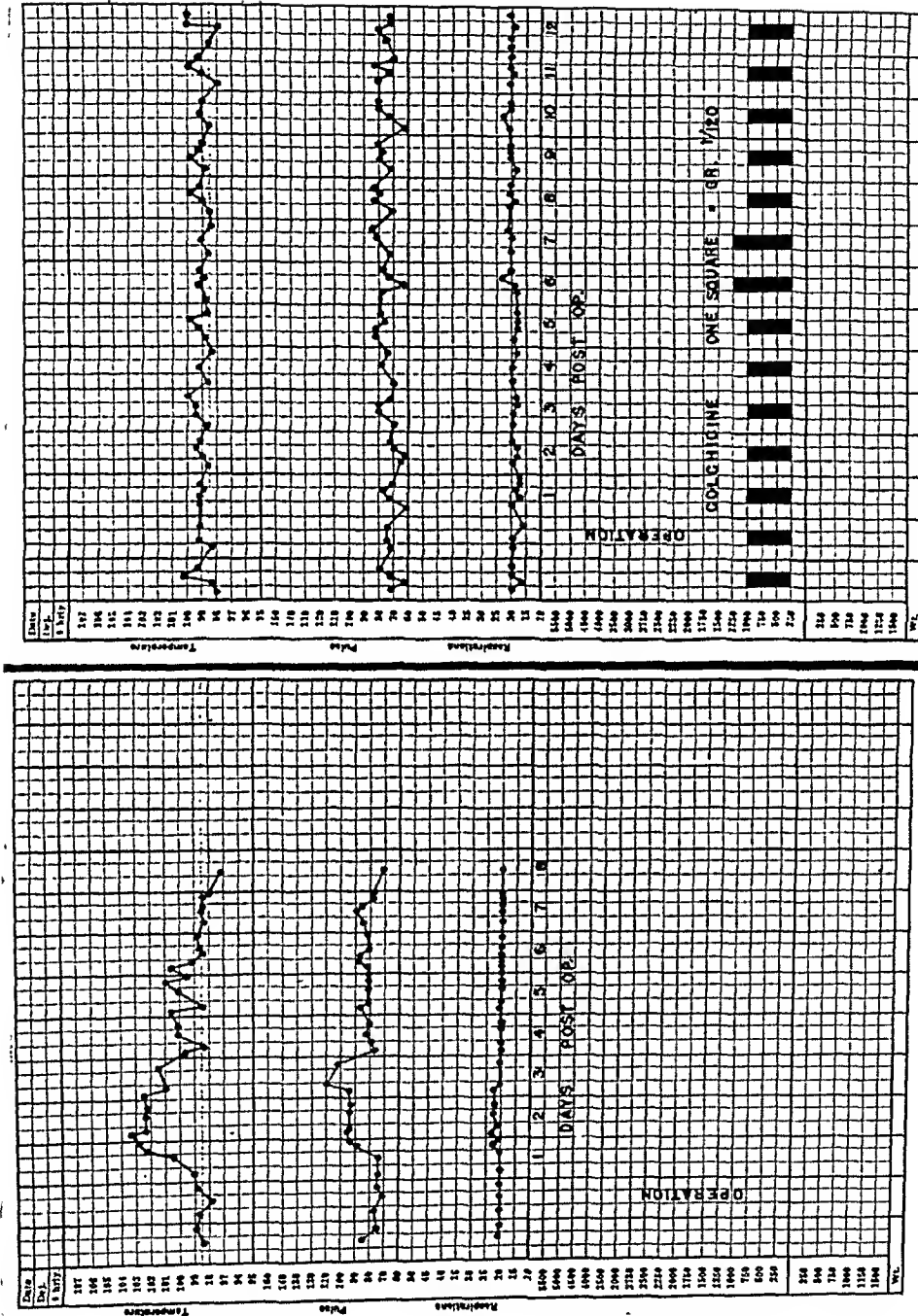


FIG. 13.—An anteroposterior roentgenographic view of the specially constructed shoe worn by the patients who had all their toes amputated for extensive tophaceous deposits. Note the forked shank of steel which is incorporated in the sole of the shoe. The shank is almost as long as the foot before amputation of the toes. This permits a spring to the patients' gait which otherwise would be lacking.

attempted. The cosmetic result (Fig. 7) was excellent and the patient received complete relief from the troublesome deposits and ulcerated lesions.

Wound Healing in Gout.—Surgical wounds in gouty patients heal exceptionally well. Ninety-three separate incisions were made in 46 operative procedures that were carried out on the 11 patients. Sepsis developed in three wounds only, and in each of them preoperative ulceration was present. The tophi had ulcerated through the skin so that operations of necessity had to be performed in the presence of infection. The sepsis was only superficial and followed removal of a tophaceous deposit involving the extensor tendons of the fingers. Two of the cases were among the earliest ones done in the period in which longitudinal skin incisions were used. It is believed that this played a part in the wound breaking down. In the third case the largest tophus of the series was removed from the dorsum of the hand, which involved all of the extensor tendons of the fingers with the exception of the thumb and fifth finger. The tophus was open and had established a sinus through the skin (Fig. 3). The removal of it necessitated such an extensive dissection of the skin overlying the tophus that its blood supply was impaired. This led to a partial slough which later required



A

B

FIG. 14.—A. The temperature, pulse and respiration chart before and after the excision of a small tophaceous deposit on the foot, under spinal anesthesia, without administration of colchicine either preoperatively or postoperatively. The patient, a male, age 62, had symptoms of gout for 20 years. Note the marked rise in temperature beginning on the first postoperative day. This was accompanied with acute joint symptoms characteristic of an acute attack of gout. The operative wound healed *per primam*, with no evidence of sepsis. B. The temperature, pulse and respiration chart before and after the removal of extensive tophaceous deposits in two fingers, under local anesthesia. The patient, a female, age 49, had symptoms of gout for 32 years. She received colchicine 1/120 grain three times a day preoperatively and postoperatively. Note the absence of any postoperative febrile reaction and, clinically, there were no signs of acute gout.

a skin graft. In two of the cases with postoperative sepsis there was bony involvement, yet no serious consequences resulted. It is worthy of note that five other cases were operated upon with open lesions, all of which healed *per primam*. The local application of sulfanilamide in the operative wounds was not used in this series of operations, but it is felt that its use would be an additional safeguard especially in cases with draining sinuses. The excellent wound healing in this group of cases suggests that sodium biurate crystals may have a bacteriostatic action since it was impossible to remove all of them from the operative wounds except in well encapsulated subcutaneous tophi. These good results do not mean that a surgeon can operate upon gouty patients as if they were normal healthy individuals but the above statistics show that one is justified in attempting to relieve patients with painful tophi without any great risk of serious infection. The only serious case of sepsis developed in the finger of one of the patients following an incision and drainage of the tophus by his local doctor, who misdiagnosed an attack of acute gout as sepsis. Neither the physician nor the patient recognized the acute attack and the incised wound was left open. This became infected subsequently and an open amputation of the finger through the proximal phalanx was required.

Postoperative Gouty Attacks.—An interesting complication may confuse the postoperative course of a gouty patient. It is not unusual on examining the clinical records of patients either with recognized or unrecognized gout to note that an unexplained fever and leukocytosis (Fig. 14) appeared on the second or third postoperative day. If the operation involved joints or was adjacent to articular structures, acute joint symptoms were prone to be attributed to the operation. If the operation was unrelated to gouty deposits the acute joint symptoms were apt to be overlooked. It is not widely appreciated that an acute attack of gout may follow any operative procedure in a gouty patient. Articular or nonarticular structures may be the site of operation. The attack may appear within 24 hours after operation or it may follow an interval of as long as a week. The attack may be monarticular or polyarticular and indistinguishable from an acute attack of gouty arthritis not related to an operative procedure.

In reviewing the records of 100 patients with gout, there were 22 operations in which no attempt was made to avert the development of postoperative gouty arthritis. The operations included a dissection of the neck for carcinoma of the esophagus, partial colectomy, radical excision of a myosarcoma of the thigh, and a Thiersch graft of the skin. The incidence of postoperative gout following this series of operations was 86 per cent. In an attempt to reduce this percentage, the ingestion of a few colchicine tablets immediately following operation was practiced. This proved successful in many instances, but eventually was extended to include preoperative as well as postoperative ingestion. At present, the routine procedure is to give three colchicine tablets ($\frac{1}{120}$ gr. each) a day for two days before operation and a similar quantity for three or more days following operation (Fig. 14).

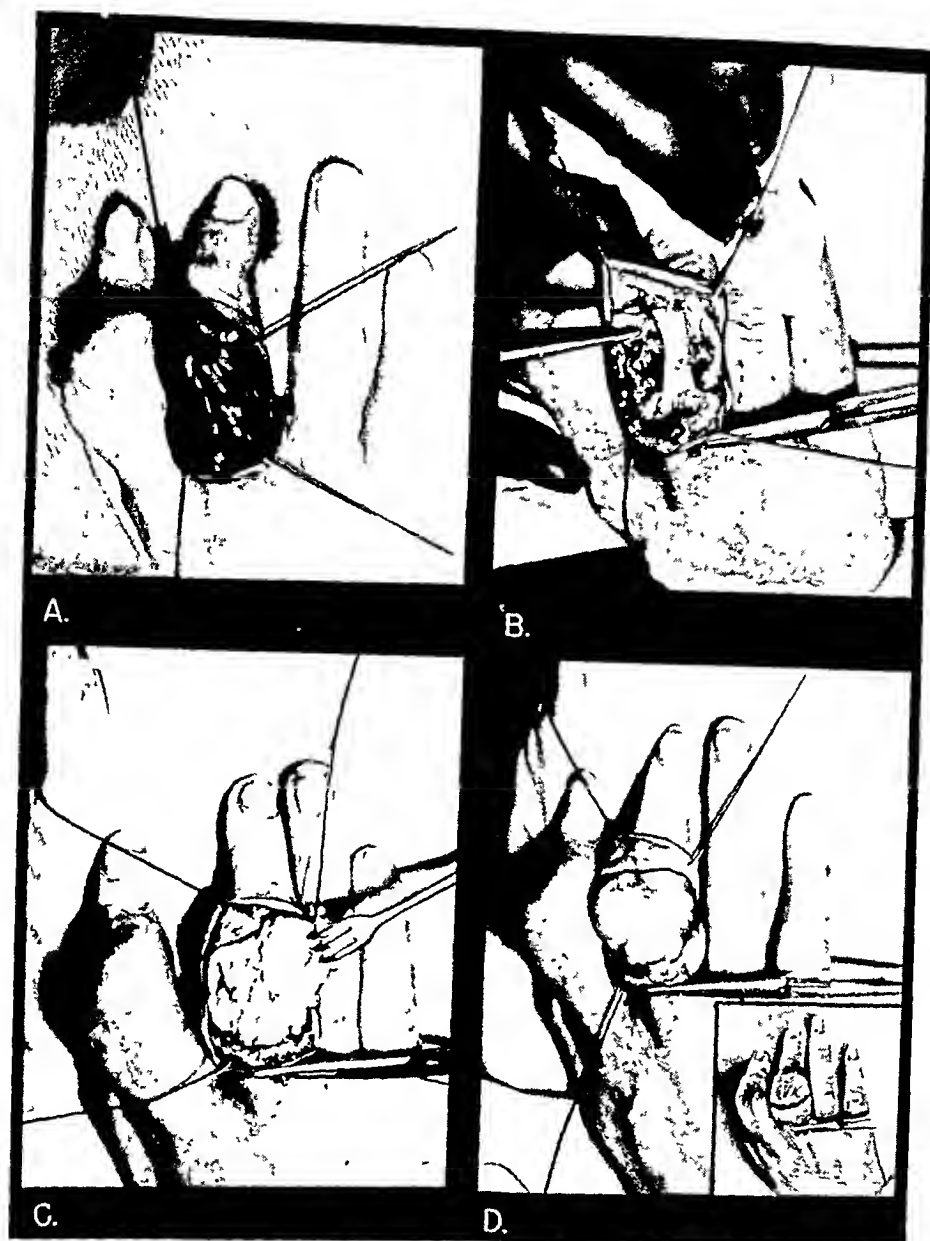


FIG. 15.—Photographs of the operative removal of an extensive tophaceous deposit involving the phalanges and tendons of the middle finger of the right hand. The patient, a female, age 49, had symptoms of gout 32 years (The same patient as in Fig. 1). The operation was performed under novocain block anesthesia at the base of the finger. (A) The skin over the tophaceous deposit has been incised, employing a transverse incision. It was dissected from the deposit with a scalpel and retracted with silk sutures. A rubber tourniquet at the base of the finger, held with the hemostat, prevented bleeding and permitted a careful dissection. Note the thin capsule of the tophus and its lobulated appearance. (B) The main mass of the tophaceous deposit has been partly freed up and pulled aside with the rake retractor. (C) More of the tophaceous deposit has been removed exposing the extensor tendon which was infiltrated with urate crystals and buried beneath the main mass of the tophus. The portion shown was preserved. The cavity beneath it represents the joint space. A considerable portion of the adjacent phalanges have been destroyed by the tophaceous deposit, leaving a large dead space after removal of the urate crystals. (D) The tourniquet has been removed. Note the free bleeding which has occurred. The skin was closed with interrupted vertical mattress sutures of silk.

A

B



C

D

FIG. 16.—The excision of large tophaceous deposits involving the left heel, the right elbow and the right first metatarsophalangeal joint. The patient, a male, age 55, had symptoms of gout for 26 years (The same patient as in Figs. 6 and 10). A. A lateral view of the heel to show the tophaceous deposit. A large piece of desquamating epidermis has been peeled downward, showing the large subcutaneous tophaceous deposit. Note the lobulated appearance of the mass and the urate crystals showing at the base of the ulcerated areas. B. The main mass of the tophus has been resected through a transverse incision, excising the ulcerated areas in the skin. The base of the wound shows normal appearing subcutaneous tissues. This tophaceous deposit did not involve a tendon or bone but lay in the subcutaneous tissues of the heel. The wound was closed with interrupted silk sutures, without drainage. The foot was immobilized in a posterior plaster shell for two weeks. The wound healed *per primam*. An excellent result was obtained (see Fig. 6). C. The skin over the olecranon has been opened through a transverse incision. The tophaceous deposit filling the olecranon bursa has been dissected from the overlying skin and the tissues beneath it and retracted downward with forceps. Note the separate deposit involving the triceps tendon in the lower portion of the wound.



G

H

D. The dissection has been carried down to the triceps tendon from which most of the tophus has been dissected away with the scalpel and curette. Some urate crystals are to be seen in the tendon. It was necessary to leave these because they had infiltrated the tendinous structure to such a degree that complete removal of them would have destroyed the attachment of the triceps tendon. The wound was closed with interrupted sutures without drainage. The elbow was immobilized with a posterior plaster splint for ten days. The wound healed *per primam*. An excellent result was obtained (see Fig. 10). E. The skin directly over the tophaceous deposit of the first metatarsophalangeal joint has been opened through a transverse incision exposing the capsule of the tophus. The skin was dissected free with a scalpel, and silk sutures in the edges were introduced for retraction to prevent undue trauma to the parchment thin skin. The lobulations of the tophus can be seen through the capsule. F. A large section of the deposit has been cut away with a scalpel, which still left a large amount of urate crystals about the bones and joint. G. The remainder of the tophus involving the base of the phalanx and the head of the metatarsal bone, and an extension of it over the dorsum of the joint to the outer side of the toe, was removed with a bone curette. The capsule of the joint was markedly infiltrated with the urate crystals, so that removal of it opened the joint space. Most of the joint cartilage and the articular ends of the bones had been destroyed but sufficient of them were intact, so that it was not felt necessary to amputate the toe. H. The wound was thoroughly flushed with normal saline solution and the skin approximated with interrupted vertical mattress sutures of fine silk, without drainage. Note the depression where the tophus had been. This cavity filled with blood clot, which became organized, resulting in a normal contour to the foot when healed (see Fig. 6). The foot and ankle were immobilized in a padded posterior plaster shell for two weeks. The wound healed *per primam*.

For this reason it was found advantageous to use local anesthesia wherever possible. Thirty-three operations in all have been performed using colchicine in prophylactic doses. The incidence of postoperative gout, in contrast to the 86 per cent among untreated patients, was only ten per cent. Gout developed in one patient who had had preoperative colchicine but not postoperatively; one had it postoperatively but not preoperatively; and one had it both preoperatively and postoperatively. It is obvious from these data that the adequate use of colchicine not only gives peace of mind to the surgeon, but comfort to the patient in the postoperative period. If a patient suddenly develops a fever in the first week following an operation, it is important to know that such a reaction not uncommonly may occur in patients with gout. More important is the recognition of the fact that it is possible to prevent attacks of postoperative gouty arthritis with adequate amounts of colchicine.

The type of anesthesia seemed to have little if any effect on the postoperative attack of gout. In this series local anesthesia with one per cent novocain infiltration was used in 24, ether in nine, spinal anesthesia in 12, and no anesthesia in one. Six of the 13 postoperative attacks of acute gout followed local anesthesia, three followed spinal anesthesia, and four followed ether anesthesia. The preponderance of cases following local anesthesia is explained by the fact that the majority of the patients received local anesthesia for their operation.

Follow-up Studies.—The follow-up studies carried out in June, 1942, or up to the death of the patients, showed that in only three out of the 93 tophaceous deposits were recurrences of any size observed. One of these was in the finger of a woman with very extensive deposits in which an inadequate removal was done at the first operation. In the second case a tophus recurred in the flexor tendon in the palm of the hand because removal had been incomplete from fear of destroying the tendon. The third case had a recurrence in the finger and was one of the earlier operations in which complete removal of the tophaceous deposit had not been obtained. The explanation of why tophi do not recur after simply removing the urate acid crystals is not offered.

Relief from pain was obtained by the surgical removal of the tophaceous deposits in all of the 11 patients. Four patients with extensive involvement of the feet, who were unable to walk without extreme pain or not at all, were rehabilitated so that they could get about without pain. Eight of the patients had painful tophi removed from the hands and fingers with marked relief of symptoms and in some with considerable restoration of function. In addition the improvement in the appearance of hands was very marked.

It is hoped that the results published in this paper will encourage others to undertake surgery in similarly afflicted gouty patients. Since this series of cases show that good results are possible by the surgical removal of tophaceous deposits, even late in life, it is recommended that surgery be done earlier in the course of the disease than usually is considered desirable.

CONCLUSIONS

1. The surgical removal of tophaceous deposits in 11 patients with gout is reported.
2. Tophaceous deposits, as a rule, primarily involve joints and secondarily tendons, bones and soft tissues, but also they may occur primarily in tendons and subcutaneous tissues.
3. Carefully planned and staged-operations may be carried out on patients with gout which result in the relief of pain, restoration of function, rehabilitation of the patient, improved cosmetic appearance, and in many instances permanent eradication of the tophaceous deposits.
4. Adequate preoperative and postoperative treatment of the patient with colchicine is essential.
5. Close cooperation between the surgeon and the internist in the selection and care of these patients is vital.

REFERENCES

- ¹ Garrod, A. B.: *The Nature and Treatment of Gout and Rheumatic Gout*. Walton & Maberly, London, 1859.
- ² Hippocrates: *Les Oracles de Cos*. Ed., Aubray, Paris, 1776.
- ³ Hutchinson: *Lectures on Some of the Surgical Aspects of Gout and Rheumatism*. Med. Press & Cir., 1880, N. S. 29, 511, and 30, 123.
- ⁴ Lindsay, J.: *Gout: Its Etiology, Pathology and Treatment*. London, 1913.
- ⁵ Llewellyn, R. L. J.: *Gout*. Wm. Heinemann, London, 1920.
- ⁶ Missaurus, P.: *The Honour of the Gout*. London, 1735.
- ⁷ Paré, A.: *Les Oeuvres*. C. & P. Rigaud fils., 10 ed., Lyon, 1641, p. 424-442.
- ⁸ Riedel: *Die entfernung der Urate und der Gelenkapsel aus dem an Podagra erkrankten Grosszehgelenke*, Deutsche Med. Wchnschr., 30, 1265, August 25, 1904.
- ⁹ Talbott, J. H.: *The Treatment of Gout*. Bull. N. Y. Acad. Med., 2nd S., 18, 318-329, May, 1942.
- ¹⁰ Talbott, J. H.: *Clinical Gout*. Rocky Mountain M. J. 38, 186-196, March, 1941.

TOTAL GASTRECTOMY FOR CANCER*

FELIX DE AMESTI, M.D.

SANTIAGO, CHILE

PROFESSOR OF SURGERY, UNIVERSITY OF SANTIAGO

THE CURE OF GASTRIC CANCER can only be achieved by surgical intervention. This end can not always be attained by mere partial resection of this organ, on account of the location of the neoplastic process or the extension of the involved area, in which case other procedures are to be contemplated, such as esophagogastrectomy or total gastrectomy.

The idea of performing a total removal of the stomach is not a new one: Already, in 1875, Czerny hinted at this possibility, which was put into practice in 1883 by the American surgeon Connor, that is, three years after Billroth had started the surgical era in the treatment of gastric cancer when he successfully performed his famed operation of a partial gastric resection. His patient died shortly after the procedure was ended, and fourteen years had to elapse before Schlatter would perform the first total gastrectomy, followed by temporary cure. Since that time there have appeared several publications, in the greatest majority of single cases or small statistics about this operation. It may be said that this procedure belongs to our day, inasmuch as it is only in the last four or five years that medical centers specialized in gastric cancer have placed it where it deserves to be. Up to date, there are about 240 total gastrectomies recorded in the literature; but this figure does not correspond nearly to the actual number of operations performed. Suffice it to say that 55 of them have been performed at the Lahey Clinic, while at the Massachusetts General Hospital this figure goes up to nearly 80. Even so, it is our feeling that it is not performed as frequently as it should be, which might be accounted for by the fact that patients suffering from this disease are treated at any surgical or medical center and not in specialized institutions, as it should be, and where they have more precise knowledge and judgment about the indications and technic of the operation.

Let us review the physiopathologic and clinical bases that justify its performance. It is a well proved fact in humans, as well as in experimental animals, that the stomach is not an indispensable organ for the life of the individual. The function of reservoir for ingested food and its normal emptying is adequately filled by the jejunal loop, and as soon as adaptation to the new function takes place, patients can be fed. With certain restrictions, they put on weight and lead a normal life. The gastric secretions are not indispensable for the digestion and absorption of alimentary principles to occur in a proper way, provided that the patient or animal that has undergone the procedure be supplied with them in the proper amount and quality.

* Read before the New York Surgical Society, November 25, 1942.

As far as the chlorhydropeptic action is concerned, it has been proved in a most convincing manner that their simple exclusion from gastric secretion does not seriously affect the physiologic digestion of albumin, fats and carbohydrates. It has been stated that the lack of the stomach fatally induces pernicious or secondary anemia. The experiments of Ivy, Mann, Graham, and others have shown that extirpation of the stomach is not followed by anemia, a fact that could be verified as late as four years after total gastrectomy had been performed. On the other hand, clinical experience teaches us that secondary anemia is not frequent, or so much so as following partial gastrectomy, and that the cases which showed severe anemia always had secondary metastases with fatal termination. We know only the one instance of Moynihan's whose patient had a postoperative survival of three years and seven months and who died showing symptoms of pernicious anemia, post-mortem examination having failed to show any evidence of recurrent or metastatic cancer. The investigations of Castle and Locke, and others, enable us to state that there is no physiopathologic base to support such assumptions. They have demonstrated that in the stomach, but specially in the duodenum, certain substances are generated (intrinsic factor) which, in the face of alimentary proteins (extrinsic factor) give rise to the formation of certain materials (erythropoietic factor) which are responsible for red blood cell formation. Mere sparing of duodenal mucosa, as is the case when stomach is partially or completely resected, would, therefore, suffice to prevent anemia. It is obvious that the latter is apt to occur in gastrectomized patients since it may occur in nonoperated individuals, the former showing a greater predisposition for this condition than nonoperated subjects. It might well happen that before the operation the patient would be in a state of equilibrium in which pernicious anemia would not occur because gastric mucosa supplied the part of intrinsic factor that for some reason the duodenum was not able to produce: Gastrectomy would break this equilibrium and pernicious anemia would develop since the duodenal factor proves to be insufficient. This is our possible explanation of the above mentioned instance of Moynihan's patient.

Other serious objections have been made to total gastrectomy: That the mortality is very high, that the greatest majority of those who survive die very shortly after, due to recurrence, and that the very few that are spared from both the operation and the recurrence never lead a normal life due to dietary restrictions to which they are submitted. According to the first publications operative mortality has been around 50 per cent or more. However, the last ones we have been able to consult, as well as the verbal communications from surgeons in this country, specialized in this field, show that as the surgeon gets more acquainted with the operation, improves his technic and the methods of anesthesia as well as the pre- and postoperative care of the patients and, above all, when he learns to select those cases in which operation should be performed, those high mortality rate figures have

come down in a very significant proportion. In other words, the history of the mortality rate with partial gastric resection has been repeated in the case of total gastrectomy. It is estimated to be now about 15 per cent in the Lahey Clinic; and it is as low a figure as that that I have been given by Dr. Pack through his experience at the Memorial Hospital. In our own experience, the mortality has gradually decreased and in the last four, only one patient died from bronchopneumonia. These facts, together with the truism that gastric cancer untreated, or treated by other means than surgery, ends by death in 100 per cent of cases, entitles us to state that in spite of being a difficult and a formidable procedure, total gastrectomy should be performed in certain cases of gastric cancer.



FIG. 1.—Gross specimen of stomach and spleen after total gastrectomy for cancer.



FIG. 2.—Showing stasis and barium retention in the proximal jejunal limb, 24 hours after ingestion of barium, in a patient who had a total gastrectomy without entero-enterostomy between the ascending and descending jejunal limbs.

Which is the future of the patient with a total gastrectomy? It is true that a good percentage of them (I could not give the exact figure) die within the first year following the operation; but it is true also that survivals have been reported; many over two years, a few, as in the case of Moynihan and Mayo, over three years, the patient of Likov, four years, and a few days ago Dr. Cattell told me of having a patient who has surpassed the five-year period. The fact is mentioned that strictures at the gastro-esophageal anastomosis occur very frequently. This is true, since it is present in nearly 40 per cent of our survivals. We feel that this is one of the strongest objections against the procedure. One should watch very carefully the patient for this complication so as to perform dilatations whenever it be necessary. The technic is still to be perfected in this phase

of the problem; maybe the use of vitallium tubes left permanently in place could help to solve the problem. This is a field open to investigation.

CRITERIA FOR TOTAL GASTRECTOMY

According to our judgment, the indications and criteria to select cases fit for total gastrectomy should be as follows:

(1) A neoplastic lesion involving all or the greatest part of the stomach with neither extension to surrounding organs nor distant metastasis. This is the case in linitis plastica or in certain types of sarcoma, and it is exactly in these cases where the best results have been obtained.

(2) Sufficient degree of mobility of both stomach and lower end of esophagus so as to allow the complete removal of the organ and the construction of a perfect jejuno-esophageal anastomosis.

(3) A good general condition of the patient enabling him to stand such a formidable procedure.

(4) All surgeons with some experience in gastric cancer surgery are aware of the fact that a high percentage of patients with a partial gastrectomy develop a recurrence in the gastric stump. The works of Verbruggen about intramural extension of the disease show that it usually goes from three to four centimeters beyond the gross limits of the tumor. Verifications carried on in some of our patients and histologic examination of over 40 operative specimens made by Doctors Mena and Ossandon in the Pathological Laboratory of the Hospital del Salvador, Santiago de Chile, reveal the exactitude of Verbruggen's statements. According to this, and in order that removal be actually radical, the stomach wall should be sectioned three fingers breadth beyond the apparently diseased area. Unfortunately this is not always possible, especially in those cancers that extend along the lesser curvature. New growths confined to the cardia or to the distal end of the esophagus form a group quite apart, since they must be treated by esophagocardiectomy.

(5) Surgical equipment and trained team with experience in gastric cancer surgery.

These patients should be submitted to a scrupulous pre- and postoperative care, the same that should be taken in any serious surgical interference in the abdomen.

The choice of anesthesia is important, since it will be necessary to accomplish a most careful abdominal exploration first to detect any metastatic disease that should be a contraindication to the procedure and then, because if the operation is undertaken, it will always be a long and difficult procedure. We have often used local anesthesia, preceded by a good preoperative analgesia and supplemented with cyclopropane or intravenous injections of sufficient doses of pentothal; spinal anesthesia has proved to be very satisfactory in experienced hands, whether it be the continuous supplemented with pentothal or the Jones' method with nupercaine.

OPERATIVE TECHNIC

The incision we always employ, and that always gave room and exposure enough, is a left paramedian one carried from the costal margin down to one finger breadth below the umbilicus. I am going to refer only to the points that I consider of more importance in the technic of total gastrectomy, disregarding the details. In the first place, and I think that

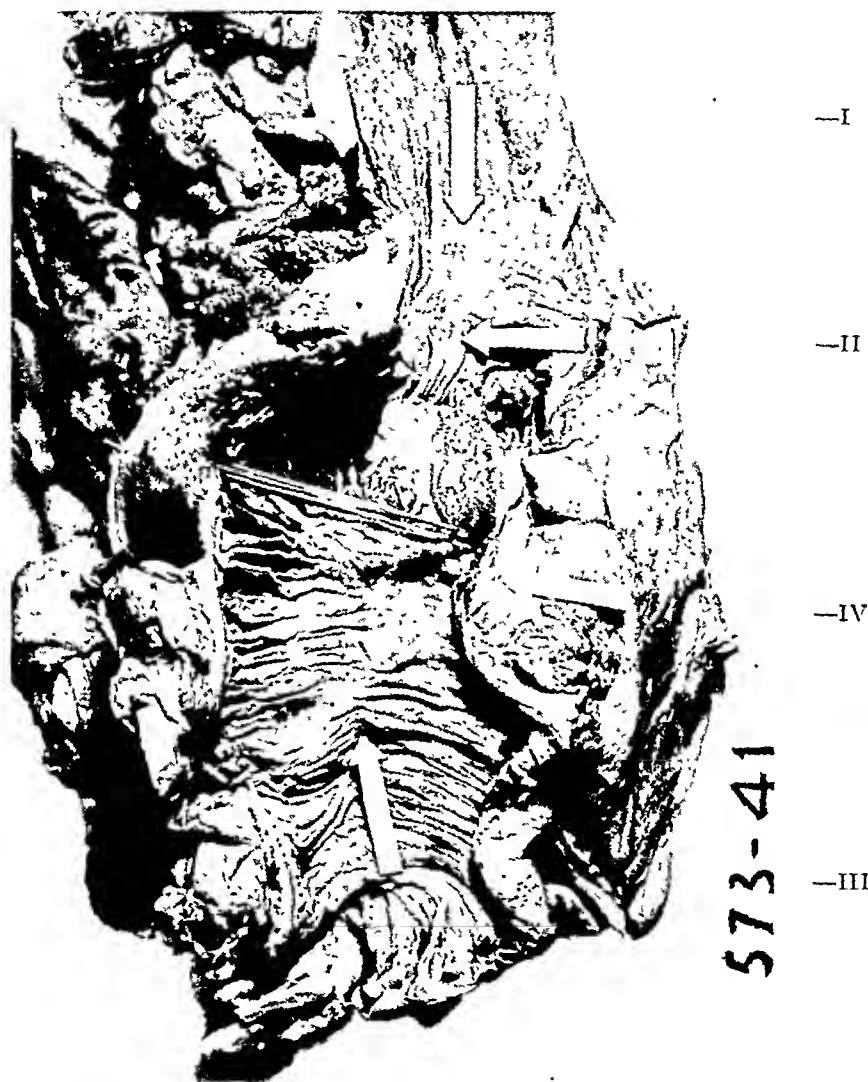


FIG. 3.—Specimen of a jejunal esophagus removed at autopsy, six months after operation.

The inferior extremity of the esophagus is anastomosed to the jejunum. The scar, product of this anastomosis, is complete. There is no loss of substance at that level. The liver, in the left lobe and on its inferior surface, appears strongly adhered to the anterior surface of the duodenum, with which it forms an oval mass.

The photograph shows both walls of the jejunum separated by a glass tube. Arrow I shows the direction of the esophagus. Arrow II marks the anastomosis of the jejunum with the esophagus. Arrow III shows the jejunum, in which are appreciated its typical folds. Arrow IV shows a piece of the left lobe of the liver adhered to the jejunum.

the agreement is unanimous, the anastomosis should be made with the jejunum rather than with the duodenum: it is of easier execution and is much less dangerous. We begin the procedure by the colo-epiploic separation, followed by clamping and tying of the gastro-epiploic vessels; on

the right side just below the duodenum, on the left side close to the lower edge of spleen; then the gastrosplenic ligament is tied in several small stumps. If this ligament appears to be involved splenectomy should be performed, which, on the other hand, renders the procedure much easier. In two of our nine patients we have had to do it; in one case for uncontrollable bleeding from the hilum; in the other for extensive involvement of the gastrosplenic ligament. Both patients survived, without any disturbance due to the removal of spleen, an experience which I have seen confirmed by several authorities. Then the pyloric artery is identified and tied and the duodenum is cut across, inverting the stump by the usual method, using the Kerr-Parker suture over a Payr's clamp. The coronary vessels are then carefully dissected and tied; the artery should be ligated very close to its origin in the celiac trunk. At the end of this stage the stomach is only held by the esophagus.

The next step should be to free the esophagus from its normal attachments to the diaphragm so as to mobilize its lower end down into the abdomen for a length of about five centimeters. To achieve this purpose several manipulations are necessary; if the left lobe of the liver is an obstacle to it, its round ligament should be sectioned, as advised by Grey Turner, and thus freed, so that it may be pushed towards the right, where it will be maintained in place by means of an abdominal retractor. Then the stomach is pulled downwards and the peritoneum is incised at the point where it reflects from the diaphragm to cover the anterior wall of the esophagus, a crescent-shaped flap being thus developed. By careful blunt dissection with the finger or a blunt dissector the esophagus is separated from the diaphragm, thus exposing both vagus nerves which, after previous novocain injection, will be cut; this will allow a further mobilization of the esophagus for about four centimeters more. The stomach is then reflected up and backwards, against the left costal margin so as to expose the posterior wall of the esophagus and perform its anastomosis with the jejunum. The first jejunal loop is then pulled up in front of the transverse colon and is anchored to the diaphragm behind the esophagus by two interrupted fine silk stitches separated one from another about five centimeters, and selecting a loop situated about 30 or 40 centimeters from the Treitz ligament. The anastomosis is performed in two layers; anterior and posterior with interrupted stitches (U-shaped) of fine silk which take support in the muscular layer of the esophagus and the serosa of the jejunum, and through-and-through continuous suture with fine chromic catgut. After these two layers have been placed, the peritoneal flap is sutured covering them with fine silk interrupted stitches.

Roscoe Graham, of Toronto, rotates the afferent loop towards the left and sutures it to the efferent loop in front of the anterior semicircumference of the anastomosis, thus, giving a peritoneal protection to the whole stoma. As he creates in this way a certain obstruction to the afferent loop, he cor-

rects it making a lateral entero-anastomosis between the two loops. It is our belief that it is always wise to perform this entero-anastomosis, regardless of whether Graham's technic is followed or not, as it facilitates the emptying of the jejunum and avoids the distension of the loop, therefore, granting a good relaxation at the level where the sutures are placed. It is advisable to pass a Levin tube through the nostril from the very beginning of the procedure, which shall be passed beyond the anastomosis down to the efferent loop. It gives an excellent rest to the stoma and enables the surgeon to feed the patient during the first eight or ten days. We employed this technic in five of our patients, and that of Graham's in the remaining four. In two of the latter group strictural changes occurred. We believe that while it makes the suturing safer it tends to stenose the anastomosis.

Our personal experience with total gastrectomy is limited to nine cases—eight carcinoma and one sarcoma, which have been operated upon between February, 1940 and May, 1942. During this interval 107 patients suffering from gastric cancer were seen, partial gastrectomy having been performed in 43 and total gastrectomy in nine; in other words, the latter operation was performed in 8.69 per cent of the total of patients and in 16.9 per cent of the gastrectomized ones.

Two of our patients were females. The age distribution was as follows: Twenty-two years, one case; 43 years, one case; from 50 to 58 years, four cases; and from 60 to 65 years, three cases.

The time elapsed between the onset of symptoms and surgical interference was from two months to one year, six cases; of one year, one case; and of two years, two cases.

Involvement of stomach by neoplastic process was as follows: Of the entire stomach, three cases; of the pylorus, one case; of the lesser curvature to the cardia, five cases.

Distribution according to histologic type showed lymphosarcoma, one; linitis plastica, three; gelatinous cancer, one; scirrhus cancer, two; adenocarcinoma, two (one of them with mucous degeneration). The eight cases of cancer showed metastases to the regional lymph nodes. The nodes present a lymphosarcoma, which were very enlarged, showed only catarrhal lymphadenitis.

According to Borrmann's classification, our cases were distributed as follows: Group I, one case; Group II, two cases, Group III, no cases; Group IV, five cases.

Four out of the nine who were operated upon died in the postoperative stage, ranging between several hours and ten days. The cause of death was peritonitis, in two cases (36 hours and six days, respectively); acute anemia (16 hours), one case; and bronchopneumonia in the last case (on the 10th day).

From the five patients who survived the operation, one died from abdominal metastases six months later, one from the same cause seven and

one-half months later, one died of unknown cause during the eleventh month, one died from inanition consecutive to cicatricial stricture of the anastomosis, proved by two repeated biopsies, and who refused to be subjected to further dilatations. Survival of 13 months has been obtained in the other case.

In two of our cases total gastrectomy was not indicated. The first was a 58-year-old woman who developed some gastric discomfort two months prior to the operation. During the operative procedure a pyloric neoplasm was found, with subpyloric metastatic lymph nodes firmly adherent to the pancreas and small enlarged nodes in the pericardial area. These were mostly subserous, and we thought them to be very probably cancerous in nature, both pyloric tumor and stomach were movable, the abdominal esophagus was unusually long, and the patient's general condition quite satisfactory. The removal was an easy one except for the dissection of the nodes adherent to the pancreas, which induced considerable bleeding. The patient died, however, in acute anemia 16 hours after the operation. Due to circumstances beyond our will, transfusion of a proper amount of blood was not administered, which might have spared this patient's life since no hemorrhage and only anemia of all viscera was found on postmortem examination. Histologic examination of the pericardial nodes showed only a catarrhal lymphadenitis; undoubtedly a frozen-section performed during procedure should have changed our whole attitude in this case.

Postmortem examination of the patient who died from bronchopneumonia demonstrated the presence of small metastases in the mesentery of the small intestine, which had passed unnoticed during exploration of abdominal cavity, and whose existence was a contraindication to the total gastrectomy.

We realize that our experience with total gastrectomy is not favorable at all, but this does not mean that we should restrain ourselves from performing it; on the contrary, it stresses the fact that through its employment it is possible to obtain long, lasting cures, provided we improve our knowledge of its precise indications and its operative technic.

PILONIDAL CYST: THE LOCAL USE OF BUFFERED SULFANILAMIDE IN PRIMARY CLOSURE

JAMES V. SCOTT,* CAPTAIN M.C., U. S. ARMY
SURGICAL SERVICE

STATION HOSPITAL, FORT BELVOIR, VA.

IT IS THE PURPOSE of this paper to present an analysis of the immediate results in wound healing of 94 cases of pilonidal cyst in which primary wound closure was attempted. All cases were operated upon by members of the Surgical Service, Station Hospital, Fort Belvoir, Va., between February, 1941, and October, 1942.

The problem of pilonidal cyst is encountered with greater frequency by the Army surgeon than by the civilian physician. In part this is due to the fact that we are dealing entirely with males of the younger age-group, but there is, in addition, the factor of increased physical activity. The patient whose pilonidal cyst has remained "dormant" during his comparably sedentary civil life may find that a short period of rigorous Army physical training, with the attendant perspiration and chafing of clothing at the upper border of the gluteal cleft, has resulted in irritation, producing an inflammatory reaction or an actual abscess. The increased incidence of direct trauma is also important. In this series of 90 white and four colored males the chief symptoms in the order of the greatest frequency were: 1. Pain. 2. Discharge. 3. Itching and skin irritation. 4. Recurrent "boil." 5. Lump. The duration of symptoms varied between one day and 17 years, the average being 21 months. A history of previous flare-up and remission was the rule. But the exacerbation, which in civil life might have been handled by rest and "local applications," and allowed spontaneously to subside, was incompatible with full military duty, and thus the patient was forced to seek early relief. All of these cases were hospitalized with one or more of the above symptoms, and no asymptomatic cysts were admitted for treatment. No cases have been included in this series in which excision was attempted elsewhere, either in a military hospital or in a civilian hospital prior to induction.

In 38 of the 94 cases infection was grossly apparent on admission to the hospital, requiring incision and drainage as the initial procedure. For this purpose we generally employed one per cent novocain local anesthesia, and made a linear incision one to two and one-half inches in length over the fluctuant area. After evacuation of the pus and cleansing of the cavity an iodoform gauze wick was inserted into the cyst cavity and allowed to protrude through the skin edges to prevent sealing of the wound. Cultures

* I wish to express my appreciation to Lieut. F. Louis Knotts, whose critical judgment is as keen as his friendship.

taken at the time of incision revealed the predominant organisms to be *Staphylococcus aureus*, *Staphylococcus albus*, *B. subtilis*, diphtheroids and gram-negative bacilli. Beginning on the first or second postoperative day hot sitz baths, two or three times daily for 30 minute intervals, afforded comfort as well as expedited the subsidence of the inflammatory process. These baths were continued, along with various topical antiseptic applications, until such time as excision was deemed advisable, determined by the gross appearance of the lesion, cessation of active drainage, and lowering of the bacterial count. The average time before excision could be undertaken was 14 days.

Fifty-six of the 94 cases did not require incision and drainage for gross infection prior to excision. For these relatively "clean" cases no routine preoperative topical therapy was employed. Some of us believe that injection of the sinus openings with methylene blue solution, done preferably one or two days prior to excision, is of advantage in outlining the diseased tissue areas.

No general agreement prevails in the literature as to the best method for handling the operative wound after removal of the cyst and sinus, and no single procedure has been without drawbacks. Kleckner's¹ report of 4,699 collected cases, of which 4,231 had been done by the open method, seems to indicate that the majority of surgeons would rather be "safe than sorry." In a review of 87 cases, Tendler² favored block dissection and open packing with iodoform gauze. He stated that in cases where primary closure was attempted "one out of three (33.3 per cent) broke down or became infected deeply." MacFee,³ in 34 primary closures, included in his review of 230 cases, reported that 18 (53 per cent) "developed abscesses or other complications which greatly prolonged the healing time." Rogers and Hall⁴ used cautery excision followed by open packing of the wound. Smith⁵ felt that "complete closure by the Lahey⁶ flap method, or any other, if successful, gives the shortest convalescence. Owing to the prolonged healing time in the wound in which infection flares up, however, the average of the group is not better than by other methods." Cutler and Zollinger⁷ opened the sinus tracts and applied a sclerosing solution. Colp⁸ anchored the wound flaps to the fascia over the sacrum and coccyx, and in MacFee's³ modification the skin itself is sutured directly to the fascia near the midline. Other forms of partial closure, undermining of flaps for better obliteration of dead space, retention sutures, and various other technics have been employed by others. Over the head of the surgeon who favors primary closure has continued to hang the scimiter of wound infection and recurrence, in spite of good results by this method, as reported by Ferguson and Mecray,⁹ and Gage.¹⁰

In this hospital we eliminated the open packing method following excision for the following reasons:

1. Prolonged hospitalization is necessary, with consequent longer absence from military duty.

2. The resulting wider, tender, thinly-epithelized scar is a discomfort to the soldier who is required to ride the hard seat of a jeep or truck, or who must assume a sitting posture with alacrity on the rifle range, and we have seen disability result from such scars split open under such stress.

3. We believe that this method is a makeshift, more useful in eliminating feared postoperative sequelae than in dealing with the primary condition.

Wound flap technics may be criticized on the basis of:

1. Prolonged hospitalization, undesirable from a military point of view.
2. Realignment of tissues at variance with their normal anatomical positions—as in the skin-to-fascia suture.
3. Deprivation of the sacrococcygeal fascia of its protective buttress of fat.

It is generally agreed that primary closure would represent the method of choice were it not for the risk of wound infection and recurrence. Statistics covering recurrence are extremely variable, so variable, in fact, that Rogers¹¹ suggestion that many so-called "recurrences" represent infected dead spaces resulting from faulty healing is not to be lightly discarded.

The technic of excision and closure we employ is as follows:

1. Under spinal procaine (100–150 mg.) or intravenous sodium pentothal anesthesia, an elliptical incision is made to encompass the entire cyst and sinus areas, but excising no more of the surrounding tissues than necessary to insure complete removal of the diseased parts. By careful dissection a minimal amount of normal skin and subcutaneous tissue is sacrificed, and, in this sense, we do not employ a true block dissection. Lateral ramifications of sinuses are dissected out in such a manner that the wound edges are not widely separated, spur incisions at right angles to the main vertical incision being made when necessary for this purpose. A wider-than-necessary cutting of the skin and subcutaneous tissues only makes closure of the wound more difficult and obliteration of the dead space more impractical. The small No. 15 Bard-Parker scalpel blade is an advantage in careful dissection, and traction on the lower or upper border of the elliptical skin edge to be excised aids in establishing a line of cleavage.

2. After removal of the diseased tissue, larger vessels are ligated with No. 00 plain catgut. Ooze is controlled by hot saline sponges. A dry wound is essential.

3. Careful inspection of the removed specimens and of the wound borders, especially the skin edges, aids in insuring that no diseased tissue remains. The greyish appearance and firm, gritty feel of a residual portion of a sinus tract or cyst wall can usually be recognized and the border of the incision extended to encompass it if present.

4. Interrupted sutures of No. 0 or No. 1 chromic catgut are placed to approximate the deep layer, the bites being taken into the lateral walls of the cavity beginning about one-half to three-quarters of an inch below the skin edge, and are anchored to the presacral fascia. These are spaced about three-fourths of an inch apart, and in such manner that each repre-

sents a simple suture, the entire circumference of which, if possible, is buried in the tissues except at the top where the knot is to be tied. We do not feel that undercutting of the fat is necessary or advantageous, since it increases bleeding, and may further reduce a none-too-adequate vascular network.

5. A sulfonamide drug preparation is sprinkled into all portions of the wound cavity. One-half to one and one-half grams of the powder is sufficient, depending upon the extent of the incision. Overuse may give rise to caking at the bottom of the wound, and may interfere with tissue healing by foreign body action, as suggested by Bick.¹²

6. The buried catgut sutures are then knotted, and they lie, at their uppermost points, about one-half to three-fourths of an inch beneath the skin margins. Placing them relatively close together aids in uniform obliteration of deep dead space, and minimal tissue excision insures that they will be tied under the least tension possible. Such buried sutures were used in 82 of this series of cases. In the remaining 12 cases the simultaneous approximation of deep and superficial tissues in one layer was attempted by the use of silk, silkworm gut or steel wire. We do not feel that such retention sutures passed through all layers, and either tied on the surface or over a gauze roll, secures as good approximation of the deep tissues, and that likelihood of introduction of infected material into the wound at the time of suture removal is greater.

7. Closure of the superficial subcutaneous tissues and skin edges is accomplished with interrupted No. 0 or No. 1 silk vertical mattress sutures (35 cases), subcuticular silk suture (13 cases), subcuticular steel alloy wire suture (15 cases), and interrupted steel alloy wire sutures (17 cases), or other suture material as dictated by the operator's preference. Absolute evenness in approximation of skin margins is important because of the proximity of the rectum and the attendant possibility of contamination from this source.

8. Sprinkling or dusting the suture line of the closed wound with a sulfonamide preparation may be an additional safeguard against surface bacteria as well as an aid in keeping the incision dry.

Postoperative attempts to obliterate potential or actual dead spaces by means of gauze rolls, pressure dressings, and placing the patient on his back may be harmful in that local circulation is interfered with. Such obliteration is better accomplished at the time of operation by the deep suture layer in the vertical plane. Consequently, we prefer a dry gauze dressing secured not too tightly by adhesive strips. This dressing is changed on the second or third postoperative day, and during the intervening time a bowel movement should not be encouraged. Purges and enemata should be avoided.

The topical application of sulfonamides to wounds, both traumatic and operative, with a view towards prevention of infection or of combating infection already present, is under thorough discussion at the moment.

The understanding of the mode of action of sulfonamides has recently made considerable progress, particularly since it was shown by Schmelkes, Wyss and associates¹³ that the anion of the sulfonamides is the agent that contributes mostly to the antibacterial effectiveness of sulfonamide solutions and that the difference between various sulfonamides is based upon the degree of their acidic dissociation. These workers drew the logical consequence from their experiments of postulating that as the p_H of the environment is increased the relative effectiveness of the stronger acids in comparison with the weaker acids would be progressively obliterated, and that actually at p_H 9 there is a very little difference mg. for mg. per cent between sulfathiazole and sulfanilamide. In view of the very much larger solubility of sulfanilamide, implantation of sulfanilamide crystals in an environment at p_H 9 should result in much more effective local chemotherapy than any other of the conventional sulfonamides.

We, therefore, obtained* a preparation of buffered sulfanilamide powder which contained ten per cent calcium carbonate in addition to the conventional crystalline sulfanilamide now in use. Calcium carbonate was used rather than soluble buffers because it was believed that in this manner buffering of the environment could be brought about that would last as long as the sulfonamide effect itself.

The following is a preliminary report of a comparative investigation of the implantation of this buffered sulfanilamide into a series of postoperate wounds obtained by the excision of pilonidal cysts:

TABLE I

Number of Cases	Drug Employed 0.5-1.5 Gm. None (controls)	Primary Healing 21 cases 72%	Infected Wounds 8 cases 27%	Average Number of Days in Hospital After Excision 24.8
29				
5	Sulfathiazole	5 cases 100%	None	22
32	Sulfanilamide	22 cases 69%	10 cases 31%	27.9
28	Buffered sulfanilamide	27 cases 96.4%	1 case 3.6%	18.8

Comment: Our criteria for classification of wounds as clean or infected was, of necessity, largely clinical rather than bacteriologic, since the presence of an abnormal number of surface organisms in this area of the body alters the validity of wound smears. Elevation of the patient's temperature, with the findings of increasing local tenderness, redness, and the spontaneous discharge or mechanical release of murky fluid or frank pus from the incision were considered significant.

* Through the courtesy of the Research Laboratories of Wallace & Tiernan Products, Inc., Belleville, N. J.

Sulfathiazole was used in only five cases because we were unable to secure an adequate supply of the drug in powdered form. The five cases are not considered to be of statistical value.

The cases in which buffered sulfanilamide was used showed a remarkably high incidence of primary healing without infection. This result can not be accounted for in any manner except by the action of the drug itself, since no other major variable in technic occurred. The percentages of each large group (Table I) requiring incision and drainage prior to excision were proportionately constant:

No drug (controls)	11 cases (38%)
Sulfanilamide	14 cases (43.7%)
Buffered sulfanilamide	12 cases (42.8%)

No systemic sulfonamide was administered except after gross infection was apparent and drainage and wound irrigations instituted. Therefore, these wounds, as far as this tabulation is concerned, may be considered to represent the local sulfonamide action only.

TABLE II

Drug Employed 0.5-1.5 Gm.	Wound Serum	Percentage of Primary Healing Groups (Table I)
None (controls).....	9 cases	31. %
Sulfanilamide.....	6 cases	27.2%
Buffered sulfanilamide.....	7 cases	25. %

In Table II are shown, under their respective groups, those wounds which healed by primary union but in which serum formation, without clinical evidence of wound infection, was detected. The percentages are comparable, and from this limited evidence we can make no deduction that either plain sulfanilamide or buffered sulfanilamide, in the quantities used, has a definite irritative foreign body action.

However, the presence of serum in clinically detectable amounts did delay healing, as can be seen when all cases are subdivided on the basis of wound status (Table III).

TABLE III
AVERAGE NUMBER OF DAYS IN HOSPITAL—94 Cases

Primary Healing Without Serum	Serum	Infection
17.9	26	40.5

It is to be remembered that when released from the hospital these cases were discharged to duty. All wounds were clinically healed at such time, although residual sensitivity of the scar to palpation and pressure was still present in most instances. We regret that the follow-up period of observation is necessarily short, and we, therefore, have no data on the question of recurrence.

Finally, the general similarity of these wounds and their anatomic location in a region of the body where wound infection is a common occurrence makes this study of the bacteriostatic effect of these drugs of some value.

SUMMARY AND CONCLUSIONS

1. Immediate results in a series of 94 cases of excision of pilonidal cyst, with primary wound closure, have been presented from the standpoint of operative technic and wound healing. We believe primary closure to be the method of choice from a military point of view.

2. The use of buffered sulfanilamide powder dusted into the wound at the time of operation has markedly reduced the percentage of postoperative wound infections, which effect plain sulfanilamide alone failed to produce.

3. The local use of buffered sulfanilamide in traumatic war wounds may be suggested from the standpoint of availability, economy and efficiency.

REFERENCES

- ¹ Kleckner, M. S.: Pilonidal Sinus: Its Surgical Management. Tr. Am. Protological Soc., 37, 166-173, 1936.
- ² Tendler, M. J.: Pilonidal Sinus. Southern Med. Jour., 34, 1156, November, 1941.
- ³ MacFee, W. F.: Pilonidal Cysts and Sinuses: A Method of Wound Closure. Review of 230 Cases. ANNALS OF SURGERY, 116, 687, November, 1942.
- ⁴ Rogers, H., and Hall, M. G.: Pilonidal Sinus: Surgical Treatment and Pathologic Structure. Arch. Surg., 31, 742-766, November, 1935.
- ⁵ Smith, M. K.: Quoted from Christopher's Textbook of Surgery: 1937, pp. 1066-1072.
- ⁶ Lahey, F. H.: An Operation for Pilonidal Sinus. Surg. Gynec. and Obst., 48, 109, 1929. *Idem*: A Further Suggestion for the Operative Treatment of Pilonidal Sinuses. Surg. Gynec. and Obst., 54, 521, 1932.
- ⁷ Cutler, E. C., and Zollinger, R.: Sclerosing Solutions in the Treatment of Cysts and Fistulae. Am. Jour. Surg., 19, 411, 1933.
- ⁸ Colp, R.: Treatment of Pilonidal Cysts and Fistulae. Surg. Clinic, North America, 9, 695, 1929.
- ⁹ Ferguson, L. K., and Mecray, P. M.: Pilonidal Cysts: Excision and Primary Suture in Ambulatory Patients. Am. Jour. Surg., 36, 270, April, 1937.
- ¹⁰ Gage, M.: Pilonidal Sinus. Transactions from Southern Surgical Assn., 1, 52, 1937. *Idem*: ANNALS OF SURGERY, 109, 291, February, 1939.
- ¹¹ Rogers, H.: The Treatment of Pilonidal Sinus in Hospital Practice. New England Jour. Med., 222, 79, January, 1940.
- ¹² Bick, E. M.: Topical Use of Sulfonamide Derivatives. J. A. M. A., 118, 511, February, 1941.
- ¹³ Schmelkes, F. C., Wyss, O., Ludwig, B. J., Marks, H. C., and Strandskow, F. B.: Mechanism of Sulfonamide Action. 1. Acidic Dissociation and Antibacterial Effect. Proc. Soc. for Exper. Biol. and Med., 50, 145, 1942.

BILIARY DYSKINESIA FROM THE SURGICAL VIEWPOINT

J. E. STRODE, M.D.

THE CLINIC

HONOLULU, T. H.

FUNCTIONAL CHANGES causing disease are in general poorly understood and frequently go undetected because of the lack of demonstrable pathologic changes at the operating table and in postmortem examinations. Dyskinesia or disorders in the motility of the extrahepatic biliary passages is an outstanding example.

Few surgeons, of wide experience in gallbladder surgery, have escaped disappointing results following cholecystectomy. This may be the case even when there is definite evidence of cholecystitis, with or without cholelithiasis. It is more particularly so when, at operation, no definite pathologic condition is found, and the gallbladder is removed because the history suggests trouble or the gallbladder visualization test suggested that the organ was not functioning properly. After the abdomen is opened it is extremely difficult, at times, to weigh all the evidence accurately that has been accumulated pre-operatively with that obtained by visual and manual examination, in determining whether or not to remove the gallbladder or explore the bile ducts. I can recall being unable to detect small stones in a normal looking gallbladder by palpation even after all the bile had been aspirated, and their presence was only demonstrated after the gallbladder was widely opened. At another time the gallbladder was removed without gross evidence of disease because of the characteristic history and because there was a small, questionable filling defect in the visualized gallbladder. On opening the removed organ a very small pedunculated adenoma was found that had undoubtedly intermittently obstructed the cystic duct. Removing the gallbladder relieved the patient of her symptoms. If doubt exists at times as to the advisability of removing the gallbladder how much more frequently the question arises as to the advisability of exploring the common duct. After the duct is opened one can never be sure that all the stones have been removed, even since the use of visualization of the biliary ducts by opaque media during the course of the operation. If symptoms of biliary colic recur following operation, doubt usually still exists as to whether or not symptoms are due to a stone having been overlooked, as to whether or not one is dealing with a functional type of biliary passage involvement, or whether or not some other organ or structure is at the bottom of the trouble.

We are familiar with the teachings of Lahey and with his insistence on exploring many more common ducts than have been explored in the past. This, in the hands of men qualified to do this type of surgery, has undoubtedly resulted in fewer instances of postoperative disappointment. It

has not, however, solved all of the problems that arise in this field of surgery.

That symptoms of gallbladder colic can occur and no stones can be demonstrated at operation, either in the extrahepatic biliary ducts or in the gallbladder, is a fact well known, and considerably written about. The first individual apparently to call attention to this was Krukenberg,¹ in 1903, and Borghi,² in 1913. In 1909, the pathologists Aschoff and Bacmeister³ contributed further to the subject by describing the "stasis gallbladder occurring without inflammation or stones." Schmieden,⁴ in 1920, wrote of the individual with gallbladder distress in whom at operation no stone or inflammation could be found and yet who showed a markedly distended gallbladder. He attributed these symptoms and findings to an anatomic defect involving the cystic duct. Berg,⁵ in 1922, suggested that biliary stasis might be the result of a functional disorder of the sphincter muscle of the ampulla of Vater, because he was able to demonstrate hypertrophy of this muscle in an individual with biliary symptoms and no other findings. Numerous investigators have interested themselves in the question of functional disorders of the biliary system. The concept that biliary distress and pain may result from motor dysfunction of the extrahepatic ducts presupposes that spasm of the sphincter mechanism about the ampulla of Vater, or perhaps elsewhere along the ducts, raises the intraductal pressure to the point where pain is produced. Distention of organs causes pain. Severe and excruciating pain occurs in Dietl's crisis when the pelvis of the kidney is suddenly distended; plugging of the cystic and common duct by stone results in severe colicky pain; distention of the intestine following obstruction gives similar symptoms. That the sphincter muscle about the ampulla of Vater is capable of resisting high intraductal pressure has been demonstrated experimentally and was strikingly evident in one of the cases which will be cited later.

Ivy⁶ has shown experimentally in dogs that the gallbladder may contract with a maximum of force of about 30 cm. of bile pressure, which is also about the secretory pressure of bile, whereas the common duct sphincter may contract and exert a resistance of as much as 80 cm. of bile pressure. Thus, it is evident in the dog, at least, that a spastic choledochoduodenal sphincter mechanism may cause an intrabiliary passage pressure sufficient to block the flow of bile either from the gallbladder or liver. Further evidence was elicited by Ivy, and his coworkers,⁷ in humans, which permitted them to conclude that "pain may be elicited from noninflamed biliary passages by the maximum pressure that may occur in their lumen provided the pressure is raised rather rapidly, especially in the presence of a tonic musculature."

To further quote Ivy, and coworkers: "This concept also provides a rational basis for gallstone colic without gallstones, for so-called 'cholecystitis,' with a normal gallbladder at operation, and for so-called 'hepatic neuralgia.' It is further possible that the presence of an irritable or hype-

trophied sphincter of the common duct may explain the recurrence of symptoms in some patients following cholecystectomy. The early relief would be due to the temporary paralysis of the sphincter that always follows cholecystectomy. But, after recovery from the temporary paralysis, the irritable or hypertrophic sphincter may again produce symptoms of biliary tract distention. The recognition of this possibility should emphasize the importance of the medical rather than the surgical management of these patients, although it must be recognized that some dyskinesia patients are benefited by cholecystectomy and some patients with residue after cholecystectomy are benefited by choledochoduodenostomy. In this connection, Aschoff⁷ reports a series of 215 cases in which 25 stone-free gallbladders were removed; of the 25, seven had residual symptoms accountable for only by dyskinetic processes. It is likely that the number of discouraging results may be fewer when the idea of a functional disturbance is better understood and managed therapeutically by the surgeon and internist. We would state, however, that we do not believe the diagnosis of dyskinesia to be simple. The presence of pain in the gallbladder region with a normal 14-hour cholecystogram, and absence of clinical evidence of an inflammatory process, may lead one to suspect but not diagnose a dyskinesia. In this communication we have desired only to emphasize that the possibility of the occurrence of biliary dyskinesia should be borne in mind and requires consideration in the etiologic analysis, diagnosis and therapy of biliary tract diseases."

McGowan, and coworkers,⁸ in 1936, interested themselves in the direct measurement of changes in physiologic function of the common bile ducts of human beings who had disease of the biliary tract. Apparently, they were the first to carry on such investigations in the human being. Individuals into whose common duct T-tubes had been placed for prolonged biliary drainage were used for their investigations; eight individuals were used and 15 observations were made. They found that giving $\frac{1}{6}$ gr. morphine subcutaneously produced an increase in intraductal pressure on 14 occasions, pressure began to rise from two and one-half to four minutes after the injection, and reached a plateau in from 10 to 15 minutes. Rise in pressure was associated with constant pain in one case. The pain was situated in the right upper abdominal quadrant and extended around the right subcostal region and to beneath the right scapula. Five attacks of pain occurred during the course of study, and in each instance was associated with a rise in intraductal pressure. The duration and severity of the pain corresponded in each case with the height of the pressure curve. On one occasion the pressure was as high as 160 mm. of water. This was the same type of pain from which the patient had suffered since removal of her gallbladder one year previously.

From their studies, the effects of morphine on the biliary system made this evidence available: "(1) Fluid can be made to flow from the common

bile duct into the duodenum after administration of morphine only by increasing the pressure. In other words, the perfusion pressure is increased. (2) Roentgenograms made before administration of morphine give evidence of rapid emptying of the common duct; the opaque medium usually is found in the duodenum. Roentgenograms of the same patients after administration of morphine give evidence of distention of the common duct. Opaque substances remain in the hepatic ducts and smaller branches of the biliary tree and the lower end of the common duct tapers to a sharp point, suggesting muscular spasm; the picture is not unlike that of the esophagus in the presence of cardiospasm. The drug that produced complete disappearance of pressure and absolute relief of pain was amyl nitrite. A few whiffs of this drug, almost at once, brought the pressure down to zero, where it remained for a few minutes and slowly returned, after about 15 minutes, to the level at which it had been after administration of the morphine. At the same time that the pressure fell, the patient was completely relieved of pain."

Strauss,⁹ and associates, in 1933, reported 29 cases of chronic biliary stasis without stones, which they believed were due to a triangular infection of the duodenum, pancreas and common duct. They thought the infection probably began as a duodenitis and ascended the common duct producing infiltration and swelling of the ampulla of Vater and lower part of the common duct, thereby causing spasm and obstruction of the papillary outlet of varying intensity. In some of these cases attacks simulating gallstone colic were produced, and in others jaundice simulating that caused by obstruction of the common duct from carcinoma of the head of the pancreas. Satisfactory results in most instances followed choledochoduodenostomy plus gastro-enterostomy. Undoubtedly, most of these cases could be classified in the category most frequently spoken of as dyskinesia of the biliary passages.

From this citation of the evidence accumulated by the above investigators and clinicians, it is evident that a typical picture of gallstone colic can be produced when no stones are present, either in the gallbladder or biliary ducts. Those are the cases in which the surgeon at the time of operation may be very much in doubt as to what course to pursue. His decision usually takes one of three directions: (1) He removes the gallbladder—perhaps explores the common duct. (2) He decides that a mistake in the diagnosis has been made, looks around for something else to account for the symptoms and, generally, winds up by taking out the appendix—meanwhile, offering up a prayer to the effect that he hopes the trouble has been found and eradicated. (3) He closes the incision and admits defeat.

Whatever the course taken, it is surprising how many people remain free of further symptoms. An indefinite percentage of the cases continue to complain of symptoms the same as previous to celiotomy, and are generally then classified as being neurotic. Again, it may happen that sufficient trouble is found at operation, usually cholecystitis with cholelithiasis, even

stones in the common duct, to account for the patient's symptoms, and yet after proper correction the symptoms persist. The conclusion usually reached, and the condition usually found, if the patient is reoperated upon, is that a stone was left or had reformed in the common duct.

Such an example stands out vividly in my memory, even though it occurred a number of years ago. A woman with typical gallstone colic was operated upon. The gallbladder, containing numerous stones, was removed, the common duct was opened and numerous stones were removed from it. None remained, so far as could be ascertained. Shortly after discharge from the hospital the patient experienced severe abdominal pain suggestive of gallstone colic. Attacks recurred with increasing severity but the patient steadfastly refused further operative interferences and died suddenly in the height of a paroxysm of pain. Autopsy revealed a small stone, a few millimeters in diameter, in the ampulla of Vater.

Such a train of events may take place, however, and no stones or other pathologic condition be found to account for the symptoms. It is in such a case that one must bear in mind the possibility of a functional abnormality—so-called dyskinesia of the biliary passages. The two following case reports are illustrative, in my opinion, of such a condition:

Case 1.—Mrs. A., Queen's Hospital No. 152069, first came under my care, November 24, 1928, because of pain in the region of the gallbladder, suggesting gallbladder colic. She stated that for the past 15 to 20 years she had suffered intermittently from such attacks of pain. There had never been fever, chills or jaundice, in spite of recurrent severe attacks of pain requiring morphine for relief. She did not submit to operation until July 23, 1932. The gallbladder contained one large stone, several smaller ones, and débris. The common duct was palpated but not explored. The gallbladder was removed. Twelve days after operation the same type of abdominal pain recurred, requiring morphine gr. $\frac{1}{2}$ for relief. These attacks occurred repeatedly until she was operated upon for the second time on May 21, 1935. It was our conclusion that a stone in the common duct had been overlooked. At operation, the common duct was found to be somewhat larger than normal, but not markedly so. The extra-hepatic ducts were thoroughly explored including probing, scooping and irrigating, and no stone could be found. A rubber ureteral bougie could be passed well down into the duodenum and, after freeing the descending duodenum and rotating it to the left, the common duct in its entirety could be palpated, but nothing abnormal could be detected. We were, again, much chagrined but equally in doubt as to the cause of our patient's disability. Symptoms were relieved for a while but soon recurred the same as before.

These attacks were unrelieved by amyl nitrite or nitroglycerin. She at no time developed clinical jaundice though the icterus index was 25 on November 10, 1939, and on May 9, 1940, it was 11 and the van den Bergh 3.25 mg. per 1,000 cc. All types of examinations were made, including gastro-intestinal, urinary, blood tests for lues, *etc.*, to explain the attacks of pain, but were all negative. The pain was so typical of biliary trouble—epigastric and right upper quadrant, radiating to back, and of such increasing severity, we felt justified in again exploring the common duct. This was done February 9, 1942. Needless to say, the procedure was difficult because of many adhesions from the two previous operations. The common duct, which was somewhat larger than normal, was again opened and explored, as well as the hepatic ducts, and

no stones could be found. A rubber ureteral bougie, similar to the one which had been passed into the duodenum at the previous operation, could not be made to pass the ampulla of Vater, and neither would saline injected into the duct. In order not to overlook a stone that might be lodged in the distal end of the duct, transduodenal exploration of the ampulla of Vater was decided upon. The descending part of the duodenum was freed along its lateral side, allowing mobilization of this part of the intestine. A longitudinal incision was made in the anterior wall of the duodenum over the region of the opening of the common duct (Fig. 1a). Though the interior of the duodenum contained a considerable quantity of bile, the opening of the duct could not be located. Saline was then injected into the common duct above by inserting

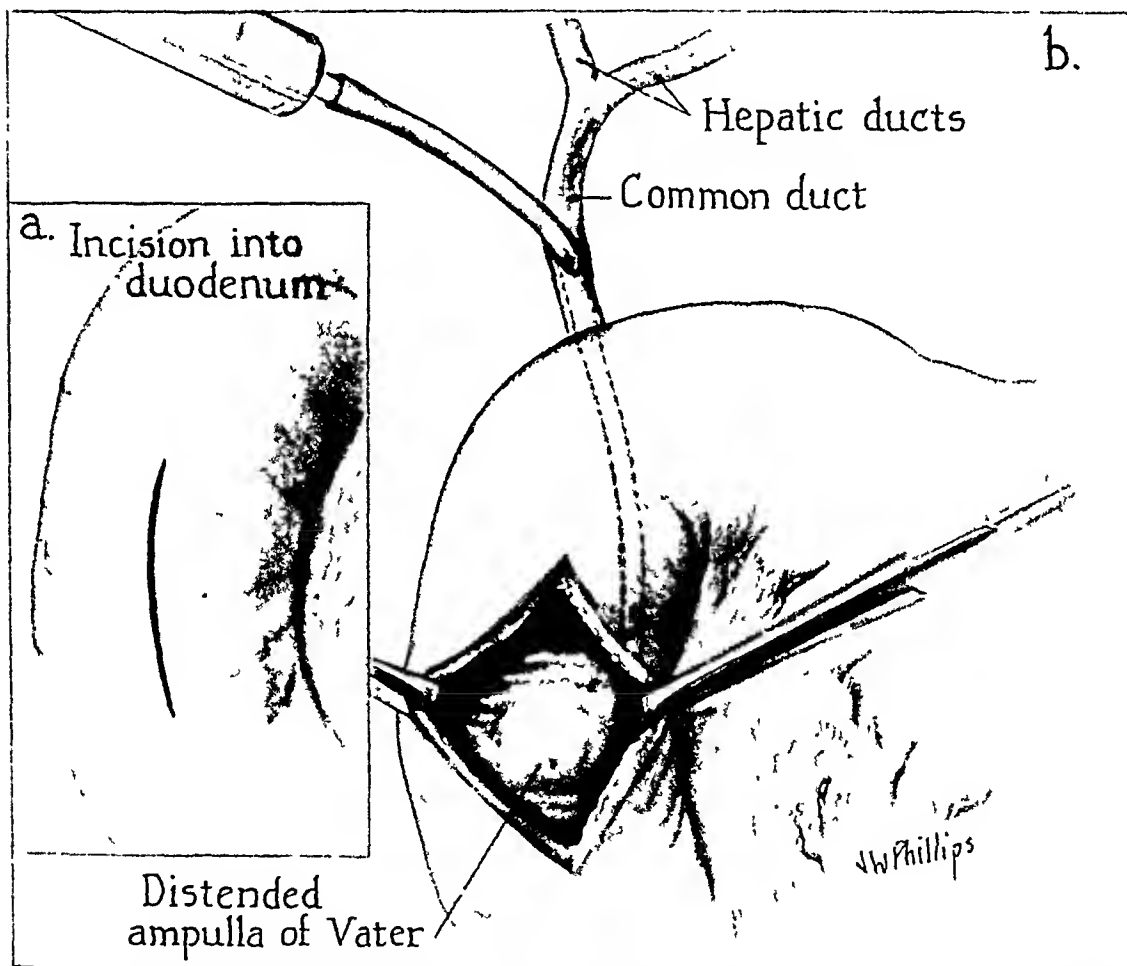


FIG. 1.—A. Shows site of incision in the duodenum to expose the opening of the common duct. B. Showing site of insertion of catheter to irrigate the common duct.

a catheter, as shown in Figure 1b, and though the region of the ampulla of Vater blew up like a balloon not a drop of saline escaped. Repeated efforts brought the same results. Since the patient had never been clinically jaundiced and there was bile present in the duodenum, it was concluded that we were dealing with a spasm (dyskinesia) of the sphincter of Oddi.

An incision was made, approximately one-half inch in length, into the ballooned-out area (Fig. 2c), and this gave a free opening into the lower end of the common duct. So far as I could determine there did not appear to be an unusual amount of hypertrophy of the sphincter muscle. However, lack of familiarity with the thickness of the normal sphincter, plus difficulty of getting a clear view because of blood and bile, made this observation of doubtful value. The common duct was now easily irrigated out, probed and scooped, and no evidence of stone could be found. The opening into the

ampulla of Vater was held open by interrupted fine chromic catgut sutures (Fig. 2d). The opening in the duodenum was sewn transversely, using a row of chromic catgut and an outer row of silk; the line of suture being covered over with a patch of omentum (Fig. 2e). The opening in the common duct was closed tight with interrupted chromic sutures. One rubber tissue drain was inserted into Morison's pouch and the incision was closed in layers. The patient made an uneventful recovery and to date (October 1, 1942) has been entirely free of gallbladder symptoms.

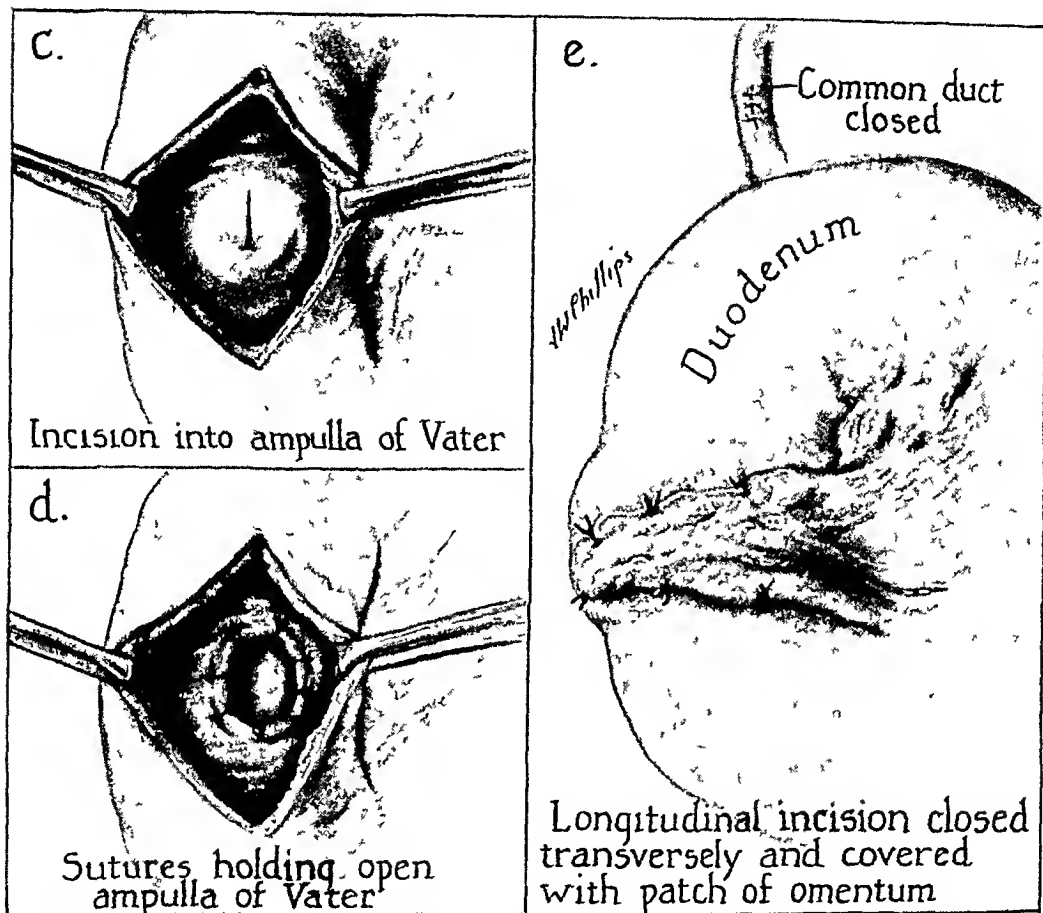


FIG. 2—C Showing the incision into the ampulla of Vater. D. Showing the technic of procedure of holding open the ampulla of Vater. E. Showing the method of protection of the incision into the duodenum.

Case 2.—A female, age 48, had had, for the past 20 years, recurrent severe attacks of epigastric pain. After the December 7, 1941, "blitz" these attacks became much more frequent and more severe. Roentgenologic examination following gallbladder visualization substantiated the diagnosis of gallbladder disease. At operation, June 1, 1942, a gallbladder containing numerous stones was removed. The common duct was explored by palpation only, since neither the history nor local findings suggested common duct stones. The second day following operation the patient stated that the same pain recurred, though it may have been that she could not differentiate this from postoperative distress. At least, very soon following operation she developed excruciating attacks of pain similar, but even more severe, than previous to operation. These attacks required repeated injections of large amounts of morphine for their relief. At no time was clinical jaundice evident. Because stone in the common duct is the most frequent cause of such symptoms, it was felt that we were probably dealing with this condition,

though dyskinesia of the sphincter of Oddi was considered largely because of our recent experience.

Exploration of the common duct was undertaken, June 2, 1942, with practically the same findings as in Case 1. The duct was not noticeably enlarged. No stones could be found. Fluid could not be made to pass into the duodenum when injected into the common duct. A soft lead probe was gently passed down the duct as far as possible in order to help identify the proper place to open the duodenum in our search for the ampulla of Vater. The ampulla was not readily identified, but with a finger in the duodenum, as a guide, the probe was gradually worked through the common duct opening. Rubber catheters of increasing size were attached to the probe, and to one another, and drawn back up the common duct. No stones were extracted and none could be washed out by irrigation. An incision was made through the ampulla to include the sphincter of Oddi which, again, did not seem unduly hypertrophied. No sutures were placed in this incision. The duodenal incision, the opening into common duct, and abdominal wall were closed as described in Case 1. The patient made a good recovery. She left the hospital on the twelfth postoperative day, and has been symptom-free to date, October 1, 1942, of all symptoms suggesting biliary colic.

In the treatment of biliary dyskinesia and other conditions attributed to an abnormality in the region of the ampulla of Vater, in which no organic lesions were demonstrable, various surgical means of correction have been advised. Removal of the gallbladder with prolonged drainage of the common duct by means of a T-tube has its advocates. Dilating the ampulla of Vater by using sounds of increasing size has been done, apparently, with success but not without unfortunate and even fatal results, due to injury of the duct, followed by retroperitoneal infection. Strauss,⁹ in the cases previously referred to, preferred choledochoduodenostomy followed by gastro-enterostomy was added to the primary operation to side-track the stream of food and lessen intraduodenal pressure, in order to minimize the danger of food regurgitating up the biliary passages. It would seem to me controversial whether the danger from a gastrojejunal ulcer developing following gastro-enterostomy might not outweigh the dangers from bile regurgitating up the biliary passages.

Colp and Doubilet¹⁰ have found that physiologic disturbances of the sphincter of Oddi bear an important relationship to certain types of acute pancreatitis, gallbladder disease, the post cholecystectomy syndrome, the dyskinesia of the biliary tract, and some forms of transient jaundice. To correct the spasm of the sphincter of Oddi they have devised an instrument (sphinctertome) which they pass down the common duct into the duodenum. It is then withdrawn until it contacts the intestinal wall. A piece is then bitten out which is supposed to include a portion of the sphincter muscle. The procedure corresponds to the blind-punch operation for prostatic hypertrophy, which preceded our present methods of visual precision. While the method worked satisfactorily in the hands of the inventors it would seem to be fraught with considerable danger due to the blindness of the maneuver.

Anastomosing the gallbladder to the stomach or duodenum may be done, and is the procedure usually carried out in the presence of jaundice thought

to be due to malignancy of the head of the pancreas. Usually the gallbladder has been removed before it becomes apparent that one is dealing with a physiologic disturbance of the sphincter of Oddi. In fact, it is a diagnosis arrived at largely by the process of exclusion.

The operation of transduodenal exploration of the ampulla of Vater and subsequent division of the sphincter of Oddi, the method employed in our two cases, is the only procedure that lends itself to arriving at a correct diagnosis. It permits of a direct visual attack on the seat of trouble and if a stone is present this can be removed and unnecessary and undesirable side-tracking operations prevented. It is not an operation to be considered lightly, for it has potential possibilities of serious complications. However, with due amount of care and caution the risks can be kept at a minimum.

SUMMARY AND CONCLUSIONS

1. Symptoms of biliary colic can and do occur in the absence of gallstones. Biliary dyskinesia must be thought of when no stones are found at exploration.

2. Dyskinesia of the biliary passage is a disease entity with which the medical profession needs to become more familiar.

Two cases of this condition are cited, with the method employed in their correction, and a short discussion of the subject in general is indulged in.

REFERENCES

- ¹ Krukenberg, H.: Über Gallenblasenkoliken ohne Gallensteine, Berl. klin. Wchnschr., 40, 660, 1903.
- ² Borghi, *loc. cit.*, Schmieden, V., and Niessen, H.: Die Erkrankungen der steinfreien extrahepatischen Gallenwege. Verhandl. d. deutsch. Gesellsch. f. innere. Med., 44, 302-354, 1932.
- ³ Aschoff, L., and Bacmeister, A.: Die Cholelithiasis. 1909, G. Fischer, Jena.
- ⁴ Schmieden, V.: Über die "Stauungsgallenblase," Zentralbl. f. Chir., 47, 1257-1261, 1920.
- ⁵ Berg, J.: Studien über die Funktion der Gallenwege unter normalen und gewissen abnormen Verhältnissen. Acta chir. Scand., Suppl. 2, 1-185, 1922.
- ⁶ Ivy, A. C.: Physiology of Gallbladder. Physiol. Rev., 14, 1-102, 1934.
- ⁷ Ivy, A. C., Voegtlin, W. L., and Greengard, H.: Physiology of Common Bile Duct: Singular Observation. J. A. M. A., 100, 1319-1320, 1933.
- ⁸ McGowan, J. M., Butsch, W. L., and Walters, W.: Pressure in the Common Bile Duct of Man: Its Relation to Pain Following Cholecystectomy. J. A. M. A., 106, 2227, June 27, 1936.
- ⁹ Strauss, A. S., Strauss, F. A., Crawford, R. A., and Strauss, H. A.: Chronic Biliary Stasis. J. A. M. A., 101, 1365, October 28, 1933.
- ¹⁰ Colp, R., and Doubilet, H.: Endocholechochal Sphincterotomy. Surg., Gynec. and Obst., 66, 882, May, 1938.

THE ADMINISTRATION OF MORPHINE AND ANTISPASMODICS IN BILIARY COLIC

R. RUSSELL BEST, M.D.,* AND J. HAROLD BARR, M.D.†

OMAHA, NEBR.

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF NEBRASKA COLLEGE OF MEDICINE, OMAHA, NEBR.

BILIARY COLIC not infrequently presents a problem which the physician or surgeon is unable to solve immediately and satisfactorily by various hypodermic measures. Inquiries among colleagues will show that it is quite customary to administer $\frac{1}{4}$ or $\frac{1}{2}$ grain of morphine for biliary colic, and if relief does not follow within 30 minutes or more, to give a second hypodermic of the morphine together with $\frac{1}{100}$ or $\frac{1}{150}$ grain of atropine. The latter will often afford relief after morphine alone has failed. This is apparently the popular method of administering hypodermics for biliary colic whether the gallbladder is present or has been removed.

One of us, (R. R. B.^{3,4}) reported, in 1936, on the use of nitroglycerin in spastic biliary dyssynergia and with cholangiograms demonstrated the relaxing effect of nitroglycerin on the choledochal sphincter area in some cases. Butsch, McGowan and Walters⁶ reporting, in the same year, on the effects of various drugs on the choledochal sphincter area, emphasized the more immediate relaxing effect of amyl nitrite and the more lasting effect of nitroglycerin. From further experimental studies and clinical experience with morphine and antispasmodic drugs, we believe we are now able to draw more practical conclusions regarding the management of the various types of biliary colic, namely, spasm of the gallbladder, the cystic duct or the choledochal sphincter.

Since the original experiments of Kitakoji,¹³ in 1930, which were later confirmed by Lueth,¹⁶ and others, as well as by our own observations, it has been accepted that morphine and allied drugs increase the resistance of the sphincter at the lower end of the common duct. If the flow of bile is blocked by stones in the common duct, intraductal pressure rises, and in turn causes pain. Also morphine would continue to give the effect of increasing pain by contracting the sphincter mechanism, except for the fact that it tends to blot out the sensation of pain in the cerebral centers. It has been my observation among patients with severe biliary colic that many notice a sharp increase of pain for a few minutes after a hypodermic of morphine is given, but relief often follows as soon as the morphine acts on the higher nerve centers. Frequently, a second hypodermic of morphine, or morphine with atropine, is necessary before satisfactory relief is obtained. The second injection of morphine further depresses the higher nerve centers while still maintaining the spasm of the sphincter area at the lower end of the common duct, thus giving relief from pain without physiologic release

* Major, 3rd Auxiliary Surgical Group, Medical Corps, U. S. Army.

† Lieutenant, Medical Corps, U. S. Navy.

of the increased pressure in the biliary system. An antispasmodic which would be used in conjunction with morphine to consistently relax the musculature of the gallbladder, the cystic duct or the sphincter area at the lower end of the common duct, would be an efficient and reliable means of affording physiologic relief for patients with biliary colic. Experimental studies by a number of investigators have revealed no drug which is a consistent, true biliary antispasmodic in the sense of relaxing these three structures.

As for drugs which will effect relaxation of the gallbladder wall, many workers (Ivy and Bergh,¹⁰ Ivy and Oldbergh,¹¹ Johnston and Brown,¹² Lieb and McWhorter,¹⁵ and Lueth, Ivy and Kloster¹⁷) believe from their experiments and experience that atropine is effective. In a recent article, Kozoll and Necheles¹⁴ stated they could not confirm the relaxing effect of atropine with small amounts, but they did see a decreased tonus rhythm. The musculature of the cystic duct probably relaxes with the gallbladder musculature. Trasentin seems to have a relaxing effect on the gallbladder similar to that of atropine. Lieb and McWhorter, in 1915, came to the conclusion that the nitrites relaxed the isolated gallbladder musculature. They felt that morphine had no significant effect upon this structure, and the same opinion is held by other authors.

In analyzing the sphincter mechanism of the lower end of the common duct, we must consider a group of separate circular fibers and also the duodenal musculature. Schwegler and Boyden,¹⁸ after describing the components of the sphincter of Oddi in great detail, state that its most important segment is a sheath of annular fibers enclosing the preampullary portion of the bile duct and that the muscle is so well developed and strategically placed as to be capable of stopping the flow of bile into the duodenum independently of the intestinal muscle. Any drug such as morphine, by producing increased tone of the duodenal musculature through which the lower end of the common duct transverses, may, in itself, be capable of blocking the lower end of the common duct, thus giving rise to increased intraductal pressure and pain. However, Boyden and Bergh, after anatomic studies of the musculature of the lower end of the common duct and duodenum, state that they would not expect the duodenal portion to play an important part in regulating the flow of bile in man. If this is true, one must deduce that morphine acts directly on the choleductal muscle fibers similarly to its action on the duodenal musculature. If this is true, then we must also consider the effect of the antispasmodics in the same light. Again, we must not lose sight of the possibility of some coordinating mechanism between these two muscular groups.

Since, at present, we have no completely satisfactory antispasmodic for the biliary tract as a whole, the drugs which are now used should be properly applied. Atropine, the most commonly used antispasmodic, does not in itself consistently relax all biliary musculature and relieve pain. By its paralyzing action on the parasympathetic nerve endings, the sympathetics (splanchnics)

which serve to relax the gallbladder are brought into play, but possibly by the law of contrary innervation, atropine may serve to contract the sphincter mechanism. It is believed that stimulation of the parasympathetics results in contraction of the gallbladder and relaxation of the sphincter. Ivy⁹ believed from his observations that atropine relaxed the sphincter mechanism in man. In 1938, one of us (R. R. B.⁴) reported that atropine did at times have a relaxing effect on the choledochal sphincter as far as symptoms and cholangiographic studies could be interpreted. Bergh¹ reported, in 1941, that atropine had no consistent effect on the choledochal sphincter mechanism in ten patients. This statement certainly corroborates our experience. In other words, there is evidence of choledochal sphincter relaxation by atropine in some cases, while in others there appears to be no relaxing effect.

The phrase "a relaxing agent" may not be exact terminology as a drug which would only raise the irritability threshold might result in an effect consistent with the assumption that the muscular fibers were not as contracted or spastic as before administration of the drug. Doubilet and Colp,⁸ following a group of interesting experiments, are definitely of the opinion that atropine does diminish the irritability of the common duct sphincter, although the resistance of the sphincter remains within the normal range. These experiments also prove quite conclusively that when hydrochloric acid reaches the duodenum in man, it increases the muscle tone of the sphincter of Oddi. This may be a factor in the inconsistency of the reports on the action of drugs in biliary tract conditions. It is interesting to note how frequently patients suffering from biliary tract disease state that sodium bicarbonate temporarily relieves milder attacks of biliary discomfort. This probably can be explained on the basis of neutralization of the acids in stomach contents before they reach the duodenum. A high acid level in the duodenum doubtless would interfere with the effect of the relaxing agent on the sphincter mechanism. Bergh and Layne,² in a recent article, further substantiate the inconsistent effect of drugs upon the sphincter of Oddi by showing that the commonly used magnesium sulphate produced sphincter relaxation in 33 out of 42 patients. Why it did not affect the other nine, is difficult to explain in the individual cases.

With this confusion of evidence on the effects of various antispasmodics, we endeavored to carry out a series of experiments in such a way that some routine method might be derived to relieve biliary colic both when the gallbladder is intact and when it has been removed. This was worked out on the assumption that most authors agree that atropine in most instances either relaxes the gallbladder and cystic duct area or raises the threshold of irritability and if the inflammatory and pathologic changes in the gallbladder or cystic duct wall are not too pronounced, some decrease in intra-gallbladder pressure will follow, or the relaxation of the cystic duct area will permit gallbladder contents to empty into the common duct. However, if there is also increased pressure in the common duct and hepatic ducts,

satisfactory relief from the distress cannot be expected until this pressure has been decreased by permitting egress of the common duct contents into the duodenum. If the gallbladder has previously been removed, relief cannot be expected until pressure within the common duct has diminished. The following groups of experiments were made on eight patients who had had previous cholecystectomy and choledochostomy with a T-tube placed in the common duct. Delayed cholangiograms taken about eight to ten days following operation showed a patent common duct in each case.

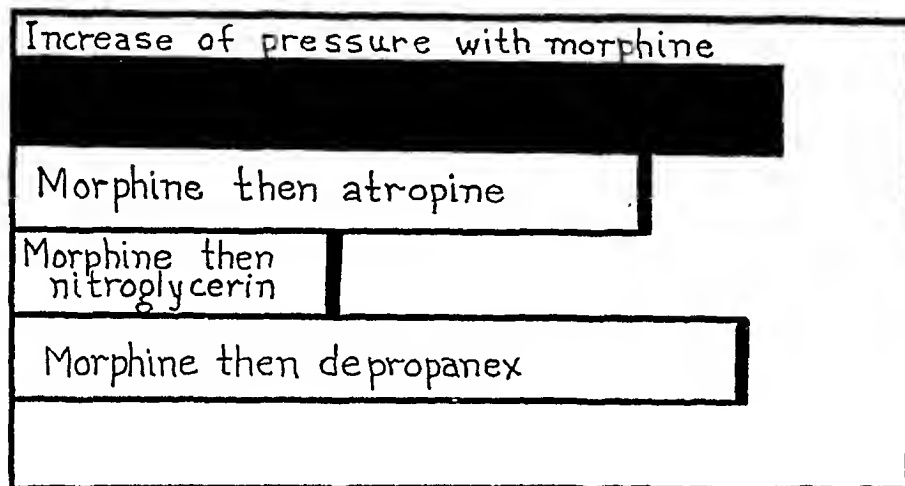


CHART 1.—The columns represent the relative heights of the average pressure levels with the various drugs. In this group, morphine was given first and then the effects of the antispasmodics were recorded with their relative decreases in intraductal pressure.

METHODS OF INVESTIGATION

A water manometer was connected to the T-tube as described in previous experiments.⁵ Briefly, the water manometer was adjusted to the estimated level of the common duct, and after filling the entire system with sterile normal saline solution from a bottle which acted as a reservoir, the normal or usual intraductal pressure of that individual was recorded in terms of millimeters of water. Readings were always taken every five minutes for at least 30 minutes. No doubt pressures vary from day to day in the individual patients, depending somewhat on their nervous state, fear, worry and exhaustion, the degree of stomach acidity, the amount, chemistry and physical properties (roughage) of their food, and upon unknown factors. On more than one occasion we have seen an increase in intraductal pressure secondary to spasm of the sphincter of Oddi caused by some rough food, such as a vegetable salad striking the gastroduodenal wall. In some such instances, the patient would have severe colicky pain. We believe a smooth diet is more frequently indicated in the management of biliary tract disease.

Three groups of readings were taken on each patient, after the effects of $\frac{1}{4}$ grain of morphine on the intraductal pressure were studied. In each case, the morphine caused an increase of the intraductal pressure varying between 10 and 280 mm. of water. In the first group, morphine was

given first (Chart 1), and within a 15- to 30-minute period, the effect of injecting either atropine, nitroglycerin or depropanex on the increased pressure, was recorded. Atropine in $\frac{1}{100}$ grain doses subcutaneously did not cause the intraductal pressure to fall back to its original level in any case, but in five instances it did appear to halt the increasing intraductal pressure at the level where it was when the atropine was injected, or at least to prevent the pressure from ascending to the height it usually reached in that particular case following injection of morphine. With nitroglycerin ($\frac{1}{100}$ grain under the tongue), five of the eight patients revealed a drop in the intraductal pressure varying from only 20 mm. of water to a marked

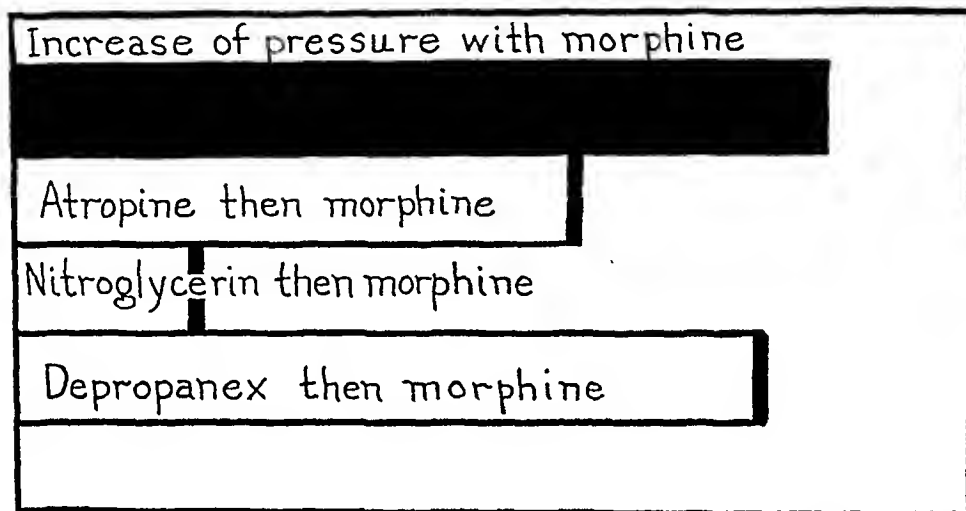


CHART. 2.—The columns represent the relative heights of the average pressure levels with the various drugs. In this group, the relaxing agent was given first, followed by an injection of morphine. As compared with Chart 1, there appears to be a definite advantage in preceding the morphine injection with the antispasmodic since the relative pressure levels are not so high as when the morphine was given first.

decrease of pressure. This decrease lasted varying lengths of time. In the other three cases, the nitroglycerin had a minimal effect on the increase of pressure brought on by the stimulation of the smooth muscle by morphine. Depropanex is a fraction of a deproteinized pancreatic extract derived from beef pancreas and was administered intramuscularly in doses of three cubic centimeters. Some investigators have found it to decrease the claudication time in certain cases of arteriosclerotic disease of the vessels of the lower extremity. Carroll and Zingdale⁷ reported, in 1938, that this extract produced relaxation of the ureters and was of definite value in cases of renal colic due to stone and in postcystoscopic colic of the ureters. In the group of eight patients studied, depropanex reduced the pressure only in two instances, and this decrease was very minimal.

In the second group of experiments, the method was reversed, the anti-spasmodic being given first, followed in about 15 minutes by an injection of morphine (Chart 2). Immediately following the injection of atropine, four of eight cases revealed a definite drop in the intraductal pressure as compared with the control readings for that patient. In all eight cases, the intraductal pressure rose following the injection of morphine, in one case

increasing as much as 120 mm. of water. In the majority of cases, however, the rise was only some 10 to 30 mm. of water. As one compares the curves in this group with those in the first series, it would seem better technic to precede the injection of morphine with atropine rather than give morphine followed by atropine. With nitroglycerin, there was a moderate to marked drop of the intraductal pressure in six out of eight cases. In the other two cases there was no drop in pressure. Then when morphine was injected, an increase resulted in four of the eight cases. As with atropine, it would appear to be more efficacious to precede the injection of morphine with nitroglycerin rather than vice versa. As for depropanex, three of the eight cases revealed a reduction in the intraductal pressure as compared with the

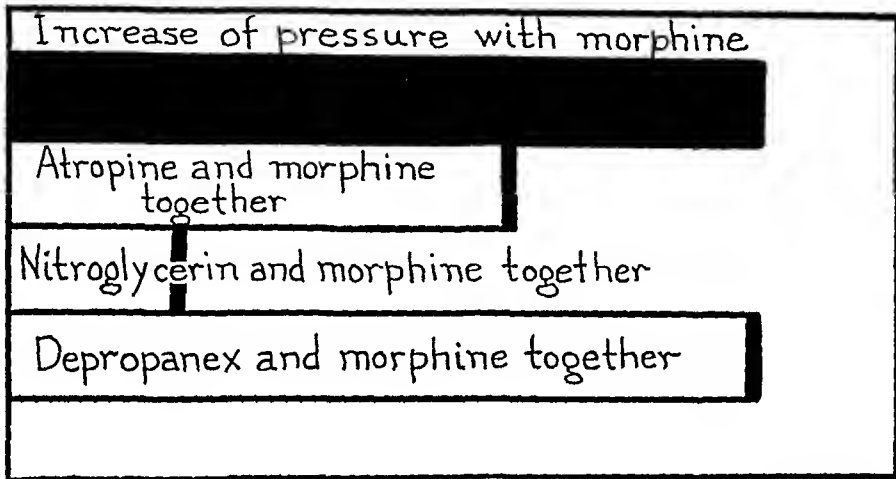


CHART 3.—The columns represent the relative heights of the average pressure levels with the various drugs. In this group, morphine and the antispasmodic were given at the same time. The relative heights of the pressure levels about parallel those of Chart 2, indicating there is no advantage in preceding the morphine with an antispasmodic as compared to giving the morphine and antispasmodic at the same time. However, there appears to be a definite advantage in giving the morphine and antispasmodic at the same time rather than giving morphine first and following it with an antispasmodic.

control for that individual. In one instance, this was very slight. As compared with atropine, it was not as efficient, but possibly slightly more prolonged in its action where its antispasmodic properties functioned. In two cases, there was even a slight increase in the intraductal pressure. When morphine followed the injection of depropanex, there was a definite rise in the intraductal pressure in all instances.

In the third group of experiments, the morphine and antispasmodics were given at the same time (Chart 3), and the intraductal pressure readings were compared with those in the previous groups. When morphine and atropine were given together, two of the cases showed a slight drop in the intraductal pressure, two showed only a minimal rise of 5 to 15 mm., and in the remaining four cases, the pressure rose 15 mm. or more. However, as a group, the curve of increased pressure was definitely less than when atropine was given following the injection of morphine, and about the same as when atropine was given preceding the morphine. With nitroglycerin placed under

the tongue at the same time as the hypodermic of morphine was given, three cases revealed a drop in intraductal pressure and in three there was a maximal rise of 5 to 15 mm. In the other two cases there was a rise of 15 mm. or more and as a group the curve of increasing pressure was far less than where the morphine was given first and followed by nitroglycerin. As compared with the experiments when nitroglycerin was first placed under the tongue and then followed by an injection of morphine, there seemed to be no advantage in prescribing it the latter way. As compared with the morphine-atropine combination, the curves were definitely in favor of the morphine-nitroglycerin combination.

In only two cases were readings taken of injecting morphine and depropanex at the same time. In both instances the depropanex did not seem to retard the increasing pressure set up by the morphine.

The drug trasentin was used in 50 mg. doses subcutaneously in three cases. The morphine and trasentin were given at the same time, and although in no case was there a drop in the intraductal pressure, the rise in pressure was minimal in two cases and moderate in one. It seems to act similarly to atropine.

SUMMARY AND CONCLUSIONS

For a patient who has the severe pain that accompanies biliary colic, morphine is definitely indicated for relief. The mechanism of this relief is the blocking effect upon the higher nerve centers but at the same time there is usually aggravation of the increasing pressure within the biliary tract which has effected the onset of pain. An antispasmodic drug which would consistently relax the gallbladder wall, the cystic duct region, and the sphincter area at the lower end of the common duct would not only hasten and prolong the relief in such cases but might also prevent further extension of the pathologic process by permitting free drainage of the biliary tract. In patients with an intact gallbladder, this biliary pain is most frequently due to increasing pressure within the gallbladder. There seems to be sufficient experimental and clinical evidence that atropine has a relaxing effect on the gallbladder wall and cystic duct or at least increases the threshold of irritability, and atropine should be given in conjunction with morphine. With a pathologic gallbladder, one cannot ascertain the status of the choledochal sphincter area. It may or may not be in a spastic state, causing increased pressure in the biliary ducts which would also contribute to the pain. Atropine could be indicated as there is experimental evidence that although this drug is inconsistent in its effect on the sphincter mechanism at the lower end of the common duct, at times it definitely relaxes the sphincter area or at least raises its threshold of irritability. Since this spastic state of the choledochal sphincter may be contributing to pain accompanying the gallbladder colic, and if the morphine-atropine combination has not given relief, morphine by hypo and nitroglycerin by mouth should then be tried 30 minutes to a few hours later because of the more marked relaxing effect of the nitro-

glycerin on the sphincter area. In any event, either atropine or nitroglycerin should be given with morphine to help counteract the tone or spasm stimulating effect of the morphine on intrabiliary pressure. (Chart 1).

In patients who have had a previous cholecystectomy, our experimental evidence and clinical experience suggests that the morphine and nitroglycerin combination should first be tried for biliary colic and if it does not afford relief, one should try a morphine-atropine injection on the assumption that in experiments, nitroglycerin could not always be depended upon to relax the sphincter area and that atropine does at times have a relaxing effect or tendency to increase the threshold of irritability of the choledochal sphincter area.

A good working rule would seem to be to try the morphine-atropine combination first in those individuals with an intact gallbladder and then alternate the atropine with nitroglycerin every four hours. Morphine should be used on the four-hour intervals only as needed. This may be continued over several days, with the hope that between the two different acting relaxing agents the gallbladder and cystic duct area would be sufficiently relaxed to permit egress of thick bile from the gallbladder into the common duct and then, in turn, the sphincter of Oddi be sufficiently relaxed to permit bile to pass into the duodenum.

In those cases where the gallbladder has been removed, the morphine-nitroglycerin combination is most apt to give relief as there is greater selectivity of nitroglycerin for relaxing the sphincter muscles than of atropine. The nitroglycerin is then alternated with atropine every four hours for several days and with the addition of morphine as necessary.

More frequently than not, when we are dealing with an individual with biliary colic and an intact gallbladder, the gallbladder obstructive phenomenon is mostly at fault, while in cases where the gallbladder has been removed, the sphincter mechanism is known to be the spastic obstructive agent.

In our experiments, depropanex was not found to be as efficient as either atropine or nitroglycerin in the management of biliary colic.

Trasentin seems to have qualities similar to atropine, but probably is not as reliable, yet it is a drug which may be used to advantage in some cases of biliary colic.

BIBLIOGRAPHY

- 1 Bergh, G. S.: The Effect of Atropine and Pilocarpine upon the Sphincter of Oddi in Human Subjects. *Proc. Am. Pharm. Soc.*, 1941.
- 2 Bergh, G. S., and Layne, J. A.: The Effect of Magnesium Sulphate upon the Sphincter of Oddi of Man. *Am. J. Digest. Dis.*, 9, 162-165, May, 1942.
- 3 Best, R. Russell, and Hicken, N. Frederick: Cholangiographic Demonstration of Biliary Dyssynergia. *J. A. M. A.*, 107, 1615-1619, November 14, 1936.
- 4 Best, R. Russell, and Hicken, N. Frederick: The Therapeutic Value of Glyceryl Trinitrate in Biliary Colic and in the Postoperative Phase of Biliary Tract Disease. *Am. J. Surg.*, 39, 533-537, March, 1938.
- 5 Best, R. Russell, Hicken, N. Frederick, and Finlayson, A. I.: The Effect of De-

TREATMENT OF BILIARY COLIC

- hydrocholic Acid upon Biliary Pressure and its Clinical Application. *ANNALS OF SURGERY*, 110, 67-80, July, 1939.
- ⁶ Butsch, W. L., McGowan, J. M., and Walters, Waltman: Clinical Studies on the Influence of Certain Drugs in Relation to Biliary Pain and to the Variations in Intrabiliary Pressure. *Surg., Gynec. & Obst.*, 63, 451-456, October, 1936.
- ⁷ Carroll, G., and Zingdale, F. G.: A Clinical and Experimental Study of the Effect of Pancreatic Tissue Extract on the Ureters. *South. M. J.*, 31, 233, March, 1938.
- ⁸ Doubilet, H., and Colp, R.: Resistance of the Sphincter of Oddi in the Human. *Surg., Gynec. & Obst.*, 64, 622-633, March, 1937.
- ⁹ Ivy, A. C.: Discussion. *J. A. M. A.*, 109, 1599, November 13, 1937.
- ¹⁰ Ivy, A. C., and Bergh, G. S.: The Applied Physiology of the Extrahepatic Biliary Tract. *J. A. M. A.*, 103, 1500-1503, 1934.
- ¹¹ Ivy, A. C., and Oldberg, E.: A Hormone Mechanism for Gallbladder Contraction and Evacuation. *Am. J. Physiol.*, 86, 599-613, 1928.
- ¹² Johnston, C. G., and Brown, C. E.: Studies of Gallbladder Function. *Surg., Gynec. & Obst.*, 54, 477-485, 1932.
- ¹³ Kitakoji, Y.: Über den Einfluss von Nervengiften auf die Funktionen der Gallenblase und der Oddischer Muskels. *Hagoya J. M. Sc.*, 5, 24-29, 1930.
- ¹⁴ Kozoll, D. D., and Necheles, H.: A Study of the Mechanics of Bile Flow. *Surg., Gynec. & Obst.*, 74, 961-967, May, 1942.
- ¹⁵ Lieb, C. C., and McWhorter, J. E.: Action of Drugs on the Isolated Gallbladder. *J. Pharmacol. & Exper. Therap.*, 7, 83-98, 1915.
- ¹⁶ Lueth, H. C.: Studies on the Flow of Bile into the Duodenum and the Existence of a Sphincter of Oddi. *Am. J. Physiol.*, 99, 237, 1931.
- ¹⁷ Lueth, H. C., Ivy, A. C., and Kloster, G.: Further Observations on the Action of Choleystokinin. *Am. J. Physiol.*, 91, 329, 1929.
- ¹⁸ Schwegler, R. A., and Boyden, E. A.: The Development of the Pars Intestinalis of the Common Bile Duct in the Human Fetus: With Special Reference to the Origin of the Ampulla of Vater and Sphincter of Oddi. *The Anatomical Record*, 68, 193-218, May, 1937.

MULTILOCULAR SEROUS CYSTS OF THE ROUND LIGAMENT SIMULATING INCARCERATED HERNIAE

REPORT OF THREE CASES

DAVID KERSHNER, M.D., AND ALFRED L. SHAPIRO, M.D.

BROOKLYN, N. Y.

FROM THE SURGICAL SERVICE, BETH-EL HOSPITAL, BROOKLYN, N. Y.

A GENUINE PRIMARY CYST of the round ligament is a rare lesion, which, when it occurs, can very readily be mistaken for an inguinal or femoral hernia. Careful perusal of standard textbooks in pathology, gynecology, and surgery, fails to reveal any mention of this condition. Since developmentally the round ligaments are derived from the caudal portions of the mesenteries of the mesonephros, and are homologous with the gubernaculum testes in the male,¹ cystic structures in this area may represent persistent embryologic rudiments. From their location it is readily understandable that they be mistaken for incarcerated inguinal or femoral herniae, with which they may be associated.

The literature is replete with reports of solid tumors, leiomyoma, adenomyoma, lipoma, endometrioma, sarcoma, and cystic degeneration of solid tumors in this area. Mayo² recently reported 11 cases of leiomyoma of the round ligament, and gave an excellent review of the literature. Hygroma or cystic lymphangioma may occur in the groin. Watson³ collected 250 such case reports of hygroma, and states that several occurred in the groin, without giving the actual number. These tumors are usually congenital, are seen shortly after birth, and grow very rapidly. They are multiloculated, thin-walled compressible cysts containing serous fluid, lined by endothelium, in contradistinction to true epithelial cysts lined by columnar or cuboidal epithelium.

Endometrial cysts of this region are infrequent, but not of great rarity. Kaulick and Gomori,⁴ in 1934, collected 3,000 cases of endometrial cysts. Of these, 60 were in the inguinal area. They added a sixty-first case, a female, age 37, with an endometrial cyst in the labium majus which they mistook for metastatic carcinoma. Beck,⁵ Fleming,⁶ and Dickinson,⁷ have all recently published single case reports of endometriosis of the round ligament. These cysts, often misdiagnosed as inguinal hernia, become swollen and tender during menstruation, conforming to the general behavior of endometriomata. Sampson⁸ called attention to the possibility of endometrial implants being carried into the groin by a hernial sac.

We have been able to find only nine case reports in the literature, four of which were histologically verified as true primary serous epithelial cysts of the round ligament. Coulson,⁹ in 1859, reported a case grossly similar, but without microscopic description. In 1896, as quoted by Cullen,¹⁰

Aschenheim described a similar instance of a walnut-sized cyst in the inguinal area attached to the uterine ligamentum rotundum, which contained a clear fluid. Here, too, the descriptive histopathology is lacking.

Martin,¹¹ in 1937, presented the case of a female, age 43, with a myomatous uterus and a mass in the right groin which was thought to be an inguinal hernia. He performed a supracervical hysterectomy and removed a cystic swelling, the size of a small tangerine, from the extraperitoneal portion of the round ligament at the abdominal ring. On examination, this proved to be a thin-walled cyst lined by low cuboidal epithelium. Schnedorf and Orr¹² report two similar cysts, both associated with indirect inguinal herniae, having single cavities lined by cuboidal epithelium with overlying loose hyaline and fibrous connective tissue. Taussig,¹³ in a review of 53 cases of tumors of the round ligament, mentions three cysts, without stating further descriptive criteria. Benchniol¹⁴ provides the most recent report of a cystic tumor of the round ligament lined by a single layer of cuboidal epithelium, surrounded by connective tissue, and containing occasional elastic fibers.

CASE REPORTS

Case 1.—Mrs. A. C., age 24, first seen June 16, 1937, complaining of a painful mass which had appeared suddenly in her right groin. Examination revealed a tender, firm, smooth swelling, 3 cm. in diameter, in the region of the right fossa ovalis. Cough elicited pain but no expansile impulse. The mass was opaque on transillumination. Because of coincident epidermophytosis, with interdigital fissuring, the initial diagnosis was acute adenitis, and conservative treatment was instituted. The patient was seen again September 18, 1937. The mass was larger and more painful at that time, but she stated that, in the interim, it had become small and had disappeared, but reappeared on straining and coughing. It disappeared again on direct pressure. Examination revealed a tender swelling, 6 cm. in diameter, situated just above the fossa ovalis, fixed to the deep structures and not freely movable. The overlying skin was reddened, but could be moved over it. The mass was irreducible, but on coughing there appeared to be a distinct expansile impulse. There was no vomiting and no evidence of intestinal obstruction. Temperature was 99.4° F.; other physical and laboratory findings were well within average limits, and irrelevant. *Preoperative Diagnosis:* Incarcerated femoral hernia.

Operative Pathology.—The subcutaneous inguinal ring was enlarged and distorted. The round ligament was unusually thick and muscular. This came through the ring as a cord, and spread out fan-wise into a cystic swelling, about 5 x 5 x 4 cm., irregular, nodular, tense, and bluish. The cyst was freed from the underlying structures. The external oblique aponeurosis was incised and the round ligament was traced back to the abdominal ring. There was no evidence of a hernial sac. The peritoneum was opened and the thick muscular round ligament was traced to its uterine attachment. There were no other cysts, and both tube and ovary were normal. The peritoneum was closed, the cyst and distal ends of the round ligament were excised, and the cut end was tacked to the undersurface of the external oblique and to the base of the inguinal ligament. The inguinal canal was reconstructed.

Pathologic Examination.—*Gross:* The specimen consists of a spherical mass 1.5 cm. in diameter with a stem 2 cm. long. The latter is a cord of loose fibrous tissue 1.5 cm. in diameter. The mass is cystic, and on section is multilocular, containing turbid, thin brown fluid. The wall is 1–2 mm. thick. The partitions are firm fibrous tissue.

The lining is irregularly finely nodular. *Microscopical*: the cyst lining is made up of a single layer of flattened cells, at times irregularly cuboidal, or of several layers of cuboidal cells. The wall is well vascularized loose fibrous tissue in which run considerable smooth muscle and a few strands of striated muscle.

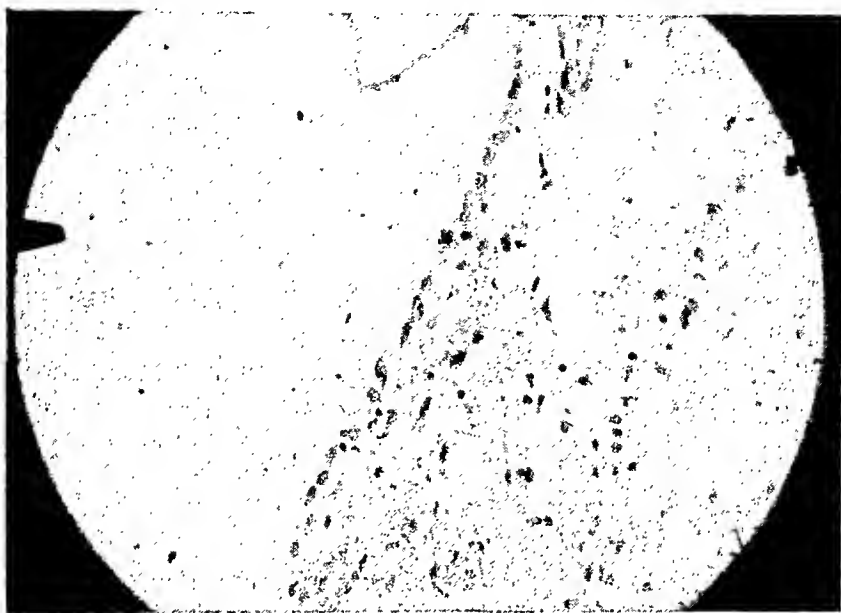


FIG. 1.—Case 2: Photomicrograph showing a multilocular serous cyst of the round ligament.

Case 2.—Mrs. R. E., age 29, first seen June 1, 1938 (service of Dr. N. Reibstein), complaining of pain and a progressively growing mass in the right groin of five months' duration. Pain was intensified on walking. Physical examination revealed a soft, irreducible egg-sized mass in the right groin, with a slight transmitted cough impulse. *Preoperative Diagnosis*: Endometrial cyst of the round ligament, although no accom-

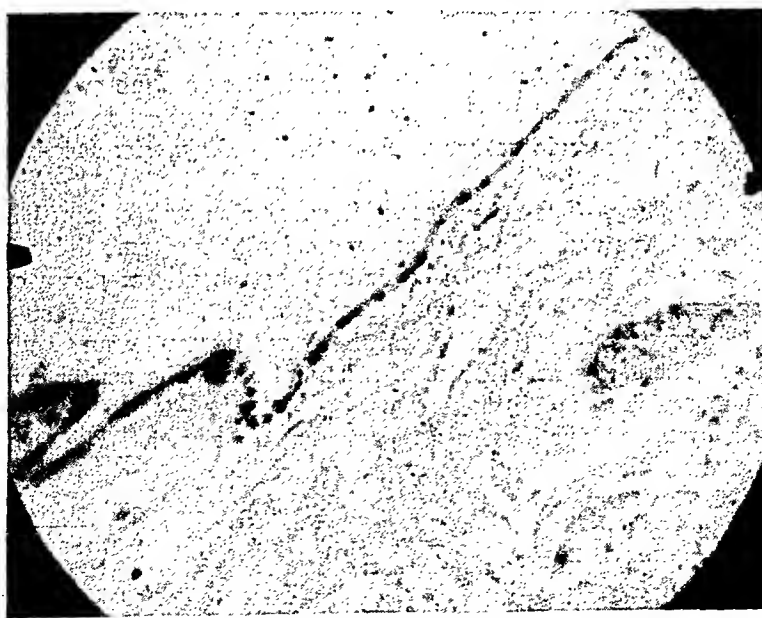


FIG. 2.—Case 2: Photomicrograph showing a multilocular serous cyst of the round ligament.

CYSTS OF ROUND LIGAMENT

panying menstrual aggravation of symptoms was noted, or inguinal hernia. *Operation.*—A cyst of the round ligament, extending into the labium minus, was excised. A coincident indirect inguinal hernia was repaired. The round ligament was clamped, ligated, and excised together with the cystic mass which was freed by blunt and sharp dissection.

Pathologic Examination.—*Gross:* The specimen consists of a mass of firm fibrofatty tissue, 10 x 2 x 4 cm., containing several small cystic spaces. *Microscopic:* Section reveals well vascularized fibro-fatty tissue with densely collagenous areas interspersed, holding several gland-like structures of varying size, lined by low columnar epithelium, ciliated, with dark cytoplasm, serous in type. Some of these are surrounded by a small amount of cellular stroma. Lining of the largest cyst is made up of a flattened cuboidal cell with a small round cell infiltration in the wall.

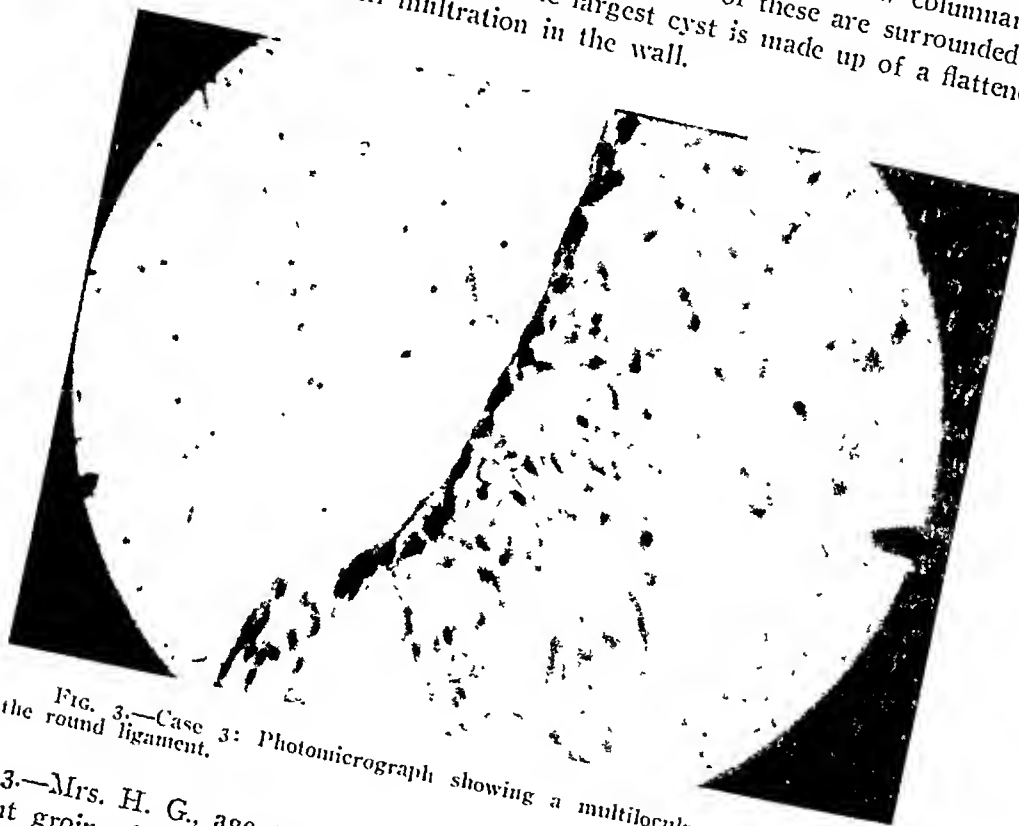


FIG. 3.—Case 3: Photomicrograph showing a multilocular serous cyst of the round ligament.

Case 3.—Mrs. H. G., age 29, first seen June 1, 1941, complaining chiefly of pain in the right groin of one week's duration. For the preceding three weeks she had noticed a persistent small lump in that region. On physical examination, a mass, 5 cm. in diameter, was noted in the region of the external inguinal ring. This was irreducible and had no expansile impulse. *Preoperative Diagnosis:* Incarcerated indirect inguinal hernia or possible endometrial cyst of the round ligament.

Operation.—A completely walled-off, multiloculated bluish cyst, 8 x 4 x 4 cm. in dimensions, was found arising from the distal end of the round ligament and protruding through the enlarged subcutaneous inguinal ring. The abdominal and pelvic peritoneum and adnexa revealed no evidence of endometriosis. The round ligament and adherent cyst were liberated and mobilized, and the distal end of the under surface of the external oblique were excised. The stump was attached to the under surface of the external oblique aponeurosis, and the inguinal canal was reconstructed.

Pathologic Examination.—*Gross:* The specimen consists of a roughly cylindrical mass of tissue, 8 x 5 x 4 cm., irregularly lobulated and cystic in feel throughout. On section, the cysts do not communicate visibly. The fluid is brownish, turbid, and odorless. The cyst wall after evacuation is smooth and dull brown and appears thin and translucent. *Microscopic:* Section shows swollen cuboidal epithelial cells with a central

large somewhat fragmented nucleus and amphophilic cytoplasm are seen to line the cyst in areas. The remainder of the wall is comprised of loose areolar tissue with bundles of smooth muscle fibers infiltrated in scattered fashion by occasional lymphocytes and plasma cells.

SUMMARY

Three cases of nonendometrial multilocular serous cyst of the round ligament simulating incarcerated herniae are reported.

REFERENCES

- ¹ Bailey, F. R., and Miller, A. M.: Textbook of Embryology. Wm. Wood & Co. New York, 1929.
- ² Mayo, C. W., and Schunke, G. B.: Leioma of the Round Ligament. *Arch. of Surg.*, **41**, 637, September, 1940.
- ³ Watson, W. L., and McCarthy, W. B.: Blood and Lymph Vessel Tumors. *Surg. Gynec. & Obst.*, **71**, 569, November, 1940.
- ⁴ Kaulick, L., and Gomori, G.: Endometriosis of the Round Ligament. *Jour. Obst. & Gynec., of Brit. Emp.*, **41**, No. 1, 63, 1934.
- ⁵ Beck, W. C.: Endometrioma in the Ligamentum Rotundum Uteri. *Am. Jour. Surg.*, **31**, 105, 1936.
- ⁶ Fleming, J. M.: Endometriosis of the Round Ligament. *Am. Jour. Obst. & Gynec.*, **38**, 598, 1939.
- ⁷ Dickinson, A. M.: Endometriosis of Round Ligament Simulating Hernia. *Am. Jour. Obst. & Gynec.*, **38**, 720, 1939.
- ⁸ Sampson, J.: Inguinal Endometriosis. *Am. Jour. of Obst. & Gynec.*, **10**, 462, 1925.
- ⁹ Coulson, A.: Cyst of the Round Ligament. *Lancet*, **2**, 113, 1859.
- ¹⁰ Cullen, T.: Adenomyoma of the Round Ligament. *Bull. Johns Hopkins Hosp.*, **7**, 112, (May-June), 1896.
- ¹¹ Martin, W. S.: Case of Cyst of the Round Ligament Simulating Inguinal Hernia. *Mich. State Med. Soc. Journ.*, **36**, 572, August, 1937.
- ¹² Schnedorf, J. G., and Orr, T. G.: Tumors of the Round Ligament of the Uterus. *Surgery*, **10**, 642, 1941.
- ¹³ Taussig, F. G.: Sarcoma of the Round Ligament of the Uterus. *Surg. Gynec. & Obst.*, **19**, 218, 1918.
- ¹⁴ Benchimiol, N. B.: Tumor Cistico do Ligamento Redondo. *Rev. Med. Cir., do Brasil*, **49**, 171, 1941.

ACUTE APPENDICITIS DURING THE LATER DECADES OF LIFE: SOME REMARKS ON THE INCIDENCE OF THE DISEASE IN A RURAL AREA

JOHN H. POWERS, M.D.*
COOPERSTOWN, N. Y.

FROM THE DEPARTMENT OF SURGERY, MARY IMOGENE BASSETT HOSPITAL, COOPERSTOWN, NEW YORK, N. Y.

INFLAMMATORY DISEASE of the vermiform appendix presents to the medical profession a constant challenge in diagnosis and management, constant because of its frequency, a challenge because of the severity and fatality of its complications and sequelae. Statistics from numerous sources show little or no reduction in mortality over a period of many years prior to the use of sulfonamides. Furthermore, in spite of modern surgical technic, recent improvements in anesthesia, and a more comprehensive knowledge of the essentials of preliminary and postoperative care, acute appendicitis, particularly during the later decades of life, still remains an exceedingly serious and often fatal disease.

It, therefore, seems appropriate to present for analysis and consideration the data on 40 patients, fifty or more years of age, with acute appendicitis and its complications, to compare these observations with similar data on 228 patients less than fifty years of age, and to draw therefrom certain deductions relative to the symptomatology, clinical course, management, and cause of death in the older group compared with the younger. All the patients have been treated at the Mary Imogene Bassett Hospital during the years 1931-1940, inclusive.

INCIDENCE OF APPENDICITIS AND ITS COMPLICATIONS

The age-composition of the population in any given community or district determines the morbidity and specific mortality of that locality. Otsego County, in which the Mary Imogene Bassett Hospital is located, is distinctly rural territory and is composed of an aging population. According to the census of 1930 the County with 16.5 per cent of its inhabitants over sixty years of age, "has already reached and probably passed the level at which, in the process of aging, the State as a whole would arrive one generation hence"¹ This fact exerts a profound influence on morbidity in Otsego County and is reflected in the age-incidence of acute appendicitis at the Bassett Hospital. For the purpose of comparing the incidence of the disease according to decades of life in this medium-sized rural institution with its incidence in two large metropolitan clinics, the age-distribution of the patients at the Bassett Hospital has been charted against similar data reported by Walker,² from the Boston City Hospital, and by Ray,³ from the New York Hospital (Chart 1). After reaching a peak during the second or third decade of life⁴ each curve falls abruptly to the fifth decade. Thereafter the curves diverge; those representing the urban cases continue to decline while that

illustrating the distribution of the rural cases remains fairly constant until the eighth decade. Expressed numerically only 3.3 per cent of the patients in Walker's series and also 3.3 per cent in the group reported by Ray were over fifty years of age, whereas, 14.9 per cent of the patients treated at the Bassett Hospital had passed the fifth decade of life. This fact is of significance in discussing the mortality of appendicitis at the latter institu-

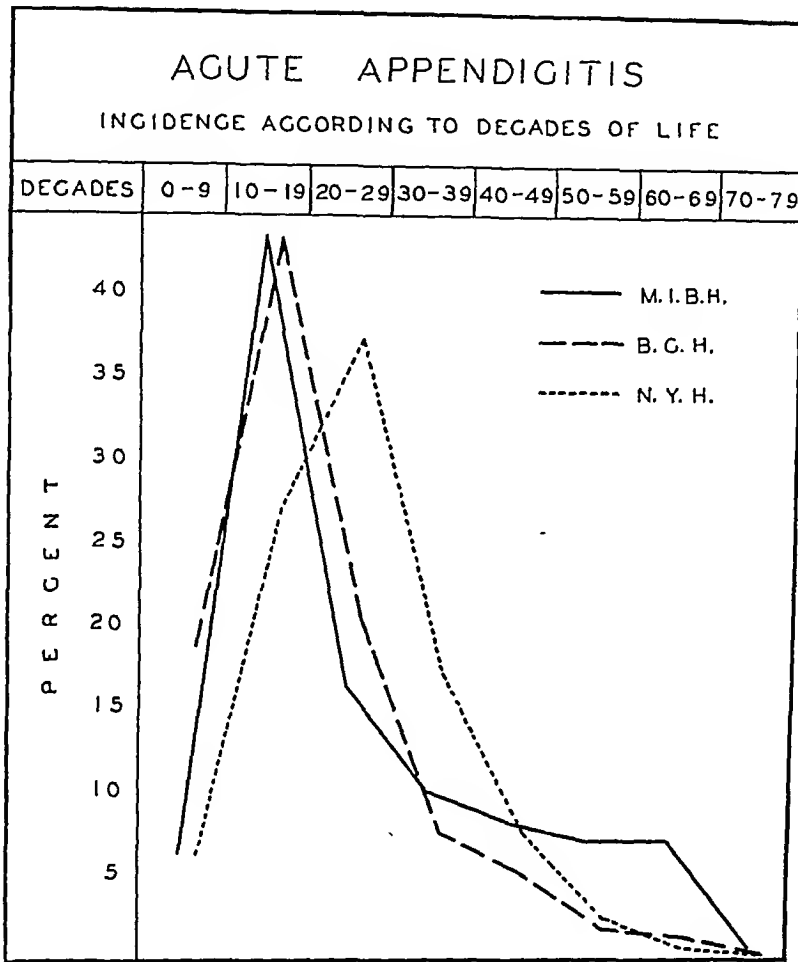


CHART I.—Incidence of acute appendicitis according to decades of life at one rural and two metropolitan hospitals.

tion and also in considering the morbidity of its complications. In older people the diagnosis of acute appendicitis is often difficult, delayed, and even unsuspected, the complications are frequent and devastating, and the mortality is high.

For the purpose of this study the classification of appendicitis suggested in the Standard Classified Nomenclature of Disease⁵ has been elaborated somewhat in order to insure accuracy in the segregation of cases according to the extent and degree of pathology present. Except a few instances in which an obvious appendiceal abscess was drained and the appendix not removed, no case has been included in which the diagnosis of acute appendicitis was not confirmed by histologic examination of the specimen. No case

TABLE I

ILLUSTRATING THE HIGHER PROPORTION OF OLDER PATIENTS AMONG THE TOTAL NUMBER WITH ADVANCED APPENDICITIS AND ITS COMPLICATIONS THAN AMONG THOSE WITHOUT PERFORATION

AGE-DISTRIBUTION OF PATIENTS ACCORDING TO SEVERITY OF DISEASE

Type of Disease	Total Patients	Per Cent Over 50 Years of Age
Acute appendicitis.....	111	5.4
Ae. ap., with gangrene.....	53	11.3
Ae. ap., with local peritonitis.....	11	9.1
Ae. ap., with perforation and local peritonitis.....	35	25.7
Ae. ap., with perforation and general peritonitis.....	25	32.0
Ae. ap., with abscess.....	33	30.3
Total.....	268	

has been classified as "acute appendicitis with perforation" unless the record contained a definite statement by the surgeon or the pathologist that a perforation existed. No case of peritonitis has been so called unless the peritoneal exudate or pus yielded a positive culture. No patient has been included in the group "acute appendicitis with perforation and general peritonitis" unless the abdominal wall was spastic throughout, the peritoneal infection generalized, according to the opinion of the operating surgeon, and the culture positive. The term "abscess" has been utilized to embrace only those cases in which the history of the illness was long and the collection of pus well localized.

In this series of cases the proportion of middle-aged and elderly people to the total number of patients with simple acute appendicitis, appendicitis with gangrene, or local peritonitis without perforation, ranged from 5.4 to 11.3 per cent. The ratio of older patients to the total number with the more advanced and serious complications of appendicitis, perforation with peritonitis, and abscess, was much higher (25.7 to 32.0 per cent) (Table I).

TABLE II

ILLUSTRATING THE HIGHER INCIDENCE OF PERFORATION WITH PERITONITIS AND ABSCESS AMONG PATIENTS IN THE LATER DECADES OF LIFE

INCIDENCE OF COMPLICATIONS AMONG YOUNG AND ELDERLY PATIENTS

Type of Disease	Under 50		Over 50	
	No.	Per Cent	No.	Per Cent
Acute appendicitis.....	105	46.5	6	15.0
Ae. ap., with gangrene.....	47	20.6	6	15.0
Ae. ap., with local peritonitis.....	10	4.3	1	2.5
Ae. ap., with perforation and local peritonitis.....	24	10.5	9	22.5
Ae. ap., with perforation and general peritonitis.....	19	8.3	8	20.0
Ae. ap., with abscess.....	23	10.0	10	25.0
Total.....	228	100.2	40	100.0

In fact, the incidence of perforation among these 40 patients who were fifty or more years of age was 67.5 per cent; among the 228 patients in the younger group the incidence was only 28.8 per cent (Table II). The serious significance of this marked variation in the frequency of perforation in these two groups is obvious, and suggests that early gangrene and dissemination of infection to the peritoneal cavity are much more frequent when appendicitis occurs after the fifth decade of life than they are prior to this age.

Furthermore, middle-aged and elderly people are less prone to tolerate operative procedures well, and are more susceptible to the hazards of anesthesia, pulmonary complications, and cardiovascular accidents, all of which must be credited against appendicitis when a fatality occurs.

DURATION OF DISEASE FROM ONSET TO ADMISSION

The reason for the high incidence of perforation with peritonitis or abscess among elderly patients has been ascribed by various authors^{4, 6, 7, 8} to delay in seeking medical attention because of frequent previous attacks of "dyspepsia," decreased "sensibility to abdominal pain," the use of some favorite "home remedy," diagnostic difficulties due to the atypical nature of the disease, the dislike of elderly people to accept advice, the "inclination to believe that old age places them beyond the hope of surgery," and various other theoretic conceptions.

TABLE III

ILLUSTRATING THE AVERAGE DURATION OF APPENDICITIS AND ITS COMPLICATIONS AMONG THE YOUNG AND OLD PATIENTS FROM ONSET OF FIRST SYMPTOM TO HOSPITALIZATION

CASES ACCORDING TO AGE OF PATIENTS, TYPE, AND DURATION OF DISEASE FROM ONSET TO ADMISSION

Type of Disease	Under 50		Over 50	
	Number of Patients	Average Length of Illness	Number of Patients	Average Length of Illness
Acute appendicitis.....	104*	33.6 hrs.	5*	31.6 hrs.
Ac. ap., with gangrene.....	47	26.4 hrs.	6	26.8 hrs.
Ac. ap., with local peritonitis.....	10	46.4 hrs.	1	22.0 hrs.
Ac. ap., with perforation and local peritonitis.....	26	49.6 hrs.	9	39.7 hrs.
Ac. ap., with perforation and general peritonitis.....	17	49.4 hrs.	8	45.6 hrs.
Ac. ap., with abscess.....	23	4.7 days	10	9.2 days

One patient excluded because duration of illness was not known.

Actually, no such delay did occur among the 40 patients over fifty years of age in this series. By ascertaining the average duration of illness from onset of the first symptom of appendicitis to arrival of the patient at the Hospital (Table III) it is apparent that, with the exception of the group "acute appendicitis with abscess," the average length of time from onset of acute appendicitis to hospitalization was 36.6 hours for the patients fifty years of age or older, and 36.0 hours for the patients under fifty. In view of the higher comparative incidence of advanced disease among the older group, (Chart 2), it is apparent that appendicitis progresses not more slowly in elderly patients, as suggested by Boyce,⁹ and Lewin¹⁰ but actually with equal rapidity. An explanation for the increased duration of illness in the older individuals with well developed appendiceal abscesses is not apparent.

One might suspect that some delay in hospitalization would be incurred by both old and young patients in country towns and farming districts because of the inconveniences of rural life, delay in obtaining a doctor, bad roads, inclement weather, and difficulties of transportation. For the purpose of comparison it is interesting to refer again to the statistics published by Walker,² and Ray.³ In Chart 3 the average duration of illness,

APPENDICITIS IN ELDERLY PATIENTS

in days, for the 268 patients in both young and old groups at the Bassett Hospital has been plotted against the same data obtained from the cases of acute appendicitis at the Boston City and New York Hospitals. It is interesting to learn that the percentage of patients reaching the Bassett Hospital during the first two days of illness was perceptibly higher than the propor-

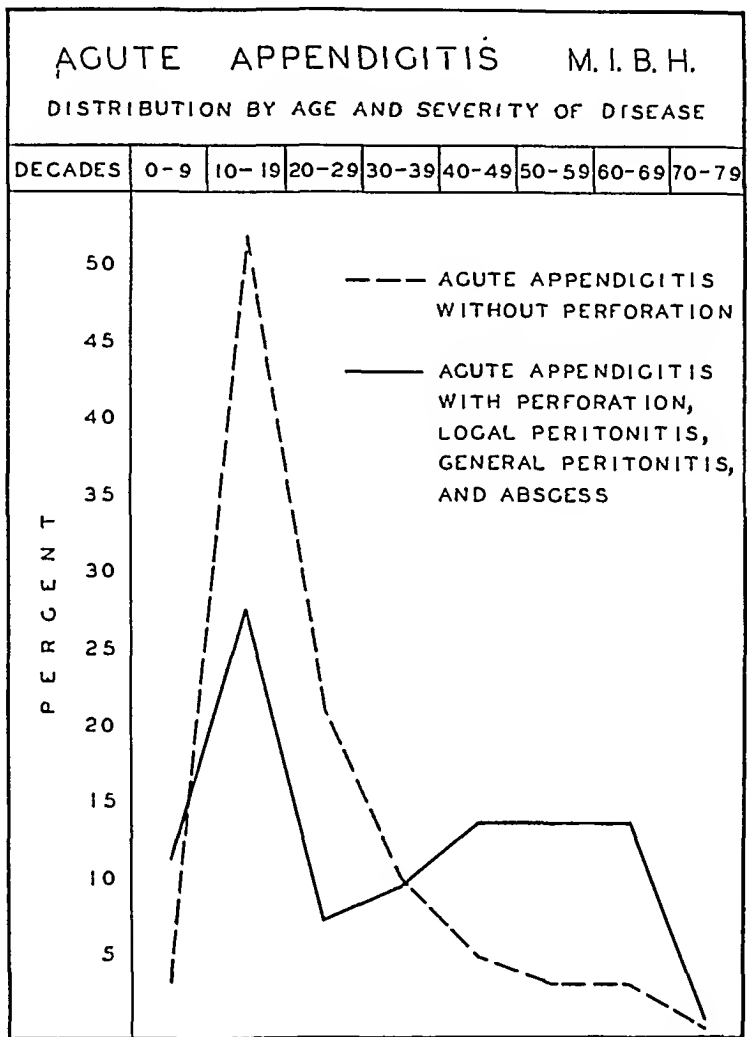


CHART 2.—Graphic illustration of the higher incidence of uncomplicated appendicitis during the second and third decades of life and the greater comparative frequency of perforation with peritonitis and abscess after the fourth decade.

tion of those arriving at the New York Hospital, and much higher than those reaching the Boston City Hospital during the same period of time, a fact highly complimentary to the diligence and skill of the medical practitioners in the towns, villages, and rural sections of Otsego and adjacent Counties.

CLINICAL FEATURES OF ACUTE APPENDICITIS IN ELDERLY PATIENTS

Much has been written about the atypical nature of acute appendicitis in elderly patients.^{7, 8, 9, 11} Maes¹² believes that “an acute attack is nearly always preceded by a story of digestive distress over a long period of time.” Maes and McFetridge¹³ go so far as to state that “any sort of symptom and any sort of circumstance can initiate appendicitis, and the disease, par-

ticularly in late adult life, can take any form at all." Obviously this statement is too broad for general acceptance. It is true, however, that the onset of appendicitis after the fifth decade of life frequently does not assume the classical triad of pain in the epigastrium followed by nausea and vomiting, with later radiation to and localization of pain in the right lower abdominal quadrant. Among those patients at the Bassett Hospital who were fifty or more years of age the first symptom of appendicitis was most commonly pain across the lower abdomen. Among the younger individuals pain in the epigastrium was usually the initial symptom, with pain in the right

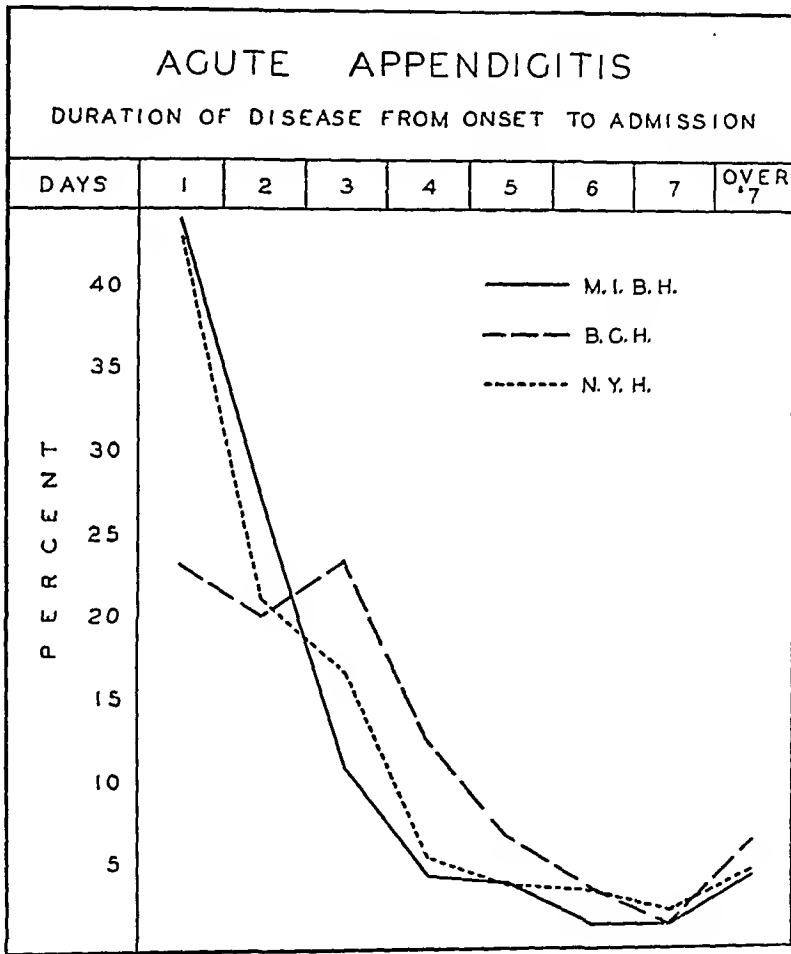


CHART 3.—Graphic representation of the duration of appendicitis among patients at one rural and two metropolitan hospitals.

lower quadrant next in order of frequency. Furthermore, among those patients who had passed the fifth decade of life the pain showed somewhat less tendency to localize in the right side. Otherwise there was no great dissimilarity between the two groups. The bizarre initial symptoms among middle-aged and elderly people which have been reported by other observers were entirely absent in this series. Also there was no prodromal period of "digestive distress," considered by Maes to be so common.

The records were frequently deficient in regard to definite historical data

APPENDICITIS IN ELDERLY PATIENTS

on the presence or absence of previous similar attacks. However, such statements were available in 191 of the patients less than fifty years of age and in 24 of the older patients. Forty per cent of the former and 46 per cent of the latter had had one or more alleged attacks of appendicitis. This difference is of little or no significance and certainly has no bearing on the more rapid progress of the disease among the patients over fifty years of age.

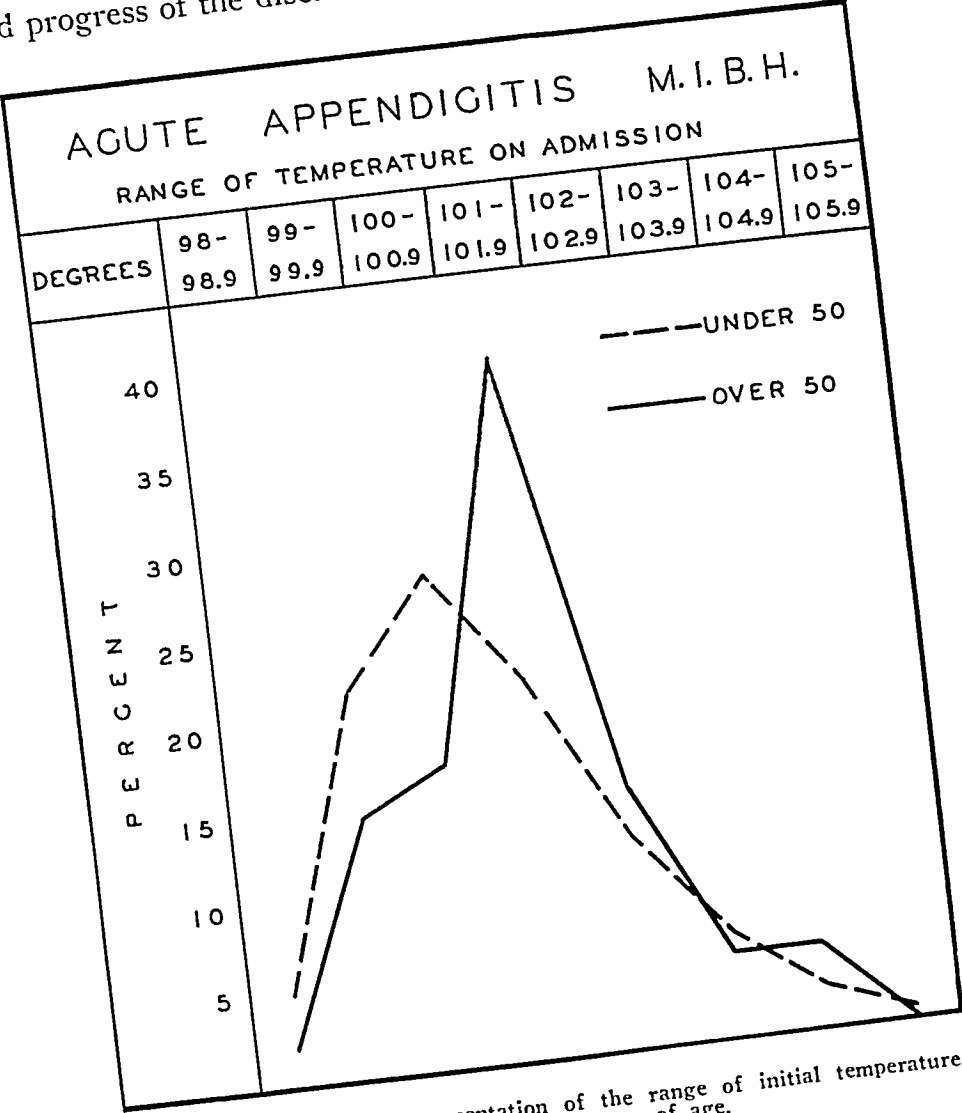


CHART 4.—Graphic representation of the range of initial temperatures among the patients under and over fifty years of age.

The records were also deficient in historical data regarding catharsis during the attack which brought the patient to the Hospital. Definite statements were made in 128 of the younger patients and 21 of the older. Of these, 51 per cent of the younger and 67 per cent of the older had taken one or more cathartics. When considered in relation to the cases in which no information was available, even though this absence of data might suggest that no cathartic had been taken, this difference is likewise probably of little significance and certainly does not account for the much higher incidence of perforation among the older patients.

There was no significant difference in the occurrence of anorexia, nausea,

vomiting, nausea and vomiting, or diarrhea in the two groups. It is interesting that 5.3 per cent of the younger patients and 7.5 per cent of the older had no gastro-intestinal disturbance of any sort.

Shaking chills were twice as common among the older patients, 15 per cent as compared with 7.9 per cent among the younger. Chilly sensations occurred with about equal frequency among the two groups.

In view of the higher incidence of generalized peritonitis among the older patients, tenderness and spasm throughout the entire abdomen were more frequent in this group; signs of localized intraperitoneal infection were more common among the younger patients. Statements regarding the presence or absence of spasm were occasionally at variance with one another.

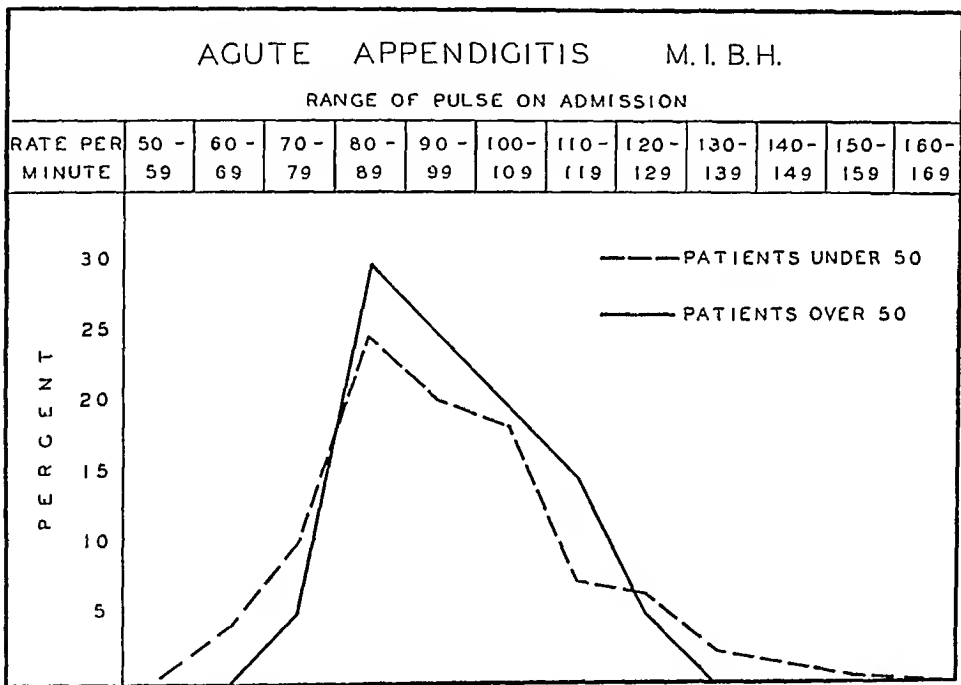


CHART 5.—Graphic illustration of the range of initial pulse rates among the young and old patients.

When any difference of opinion obtained, the statement of the older of one or more examiners was accepted as the more or most dependable. It is frequently difficult to distinguish between voluntary and involuntary rigidity of the abdominal wall, and it is also conceivable that the existence or degree of involuntary spasm may vary from time to time. Considering all these facts as possible sources of error it is, nevertheless, interesting that involuntary abdominal spasm was absent in approximately one-third of the patients in each group.

Abdominal distention was found by Wood⁸ in 55 per cent of 43 patients over sixty years of age with acute appendicitis and has been mentioned by other authors,^{14, 15} in addition to those previously cited. It is stated by some that distention may be so marked that primary intestinal obstruction due to

neoplasm, or other cause, may be suspected.¹⁶ Among the 40 patients in this series who were fifty or more years of age, abdominal distention was present only as a concomitant of peritonitis.

In brief, although acute appendicitis after the fifth decade of life may occasionally be atypical, the clinical features of the usual attack resemble rather closely those which occur earlier in life and should enable a correct diagnosis to be made in the majority of cases without undue delay.

CLINICAL PATHOLOGY

Data relative to the initial temperature, pulse rates, and leukocytic counts among the middle-aged and elderly patients compared with those in the younger group are presented graphically in Charts 4, 5, and 6. In brief, initial temperatures between 99° F. and 100.9° F. were more common among

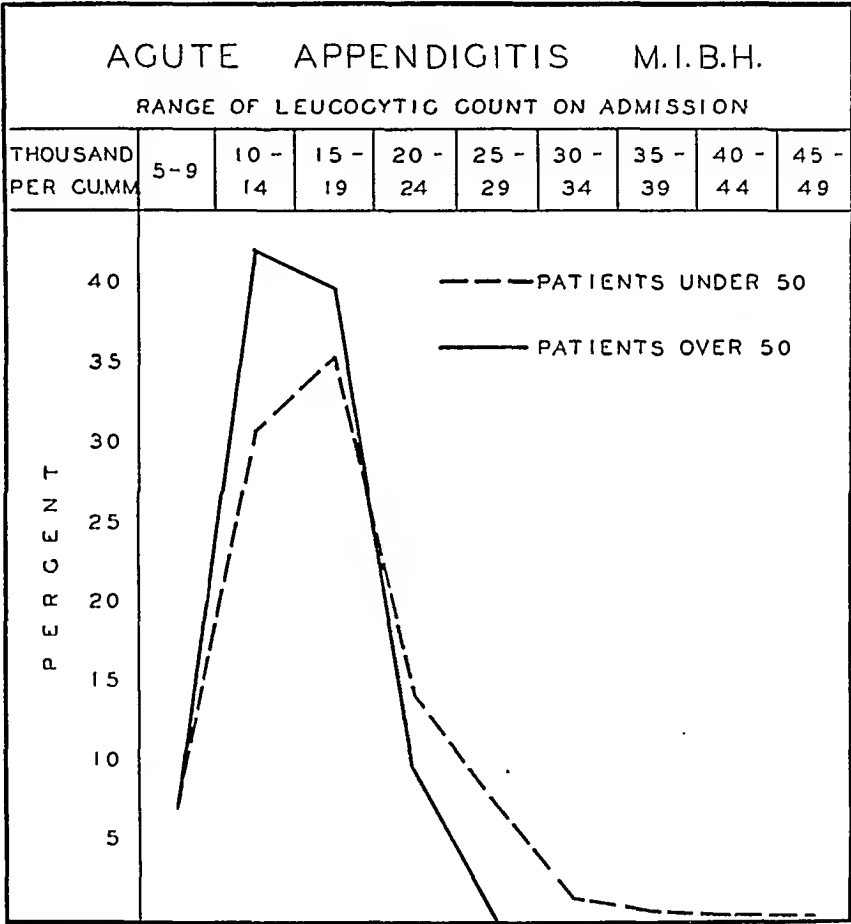


CHART 6.—Curves illustrating the variations in leukocytic counts between the two groups.

the younger patients; temperatures between 101° F. and 101.9° F. were more frequent among the individuals in the older group. In no patient over fifty years of age was the pulse rate more than 129, nor the leukocytic count above 24,000. The widest variations in both were noted among the younger patients, in some of whom the pulse rate was more than 160 and the leukocytic count above 45,000.

OPERATIVE AND PATHOLOGIC DATA

Forty-one per cent of the patients under fifty years of age were operated upon during the first two hours after admission to the Hospital, whereas only 22.5 per cent of the older patients were similarly treated during the same interval of time. In this series of cases appendicectomy with drainage was performed in 55.5 per cent of the individuals in the older group and 33.3 per cent of the younger. Drainage alone was instituted in 20 per cent of the former and 5.3 per cent of the latter. The incidence of appendicectomy with drainage for both old and young was 36.5 per cent; of drainage alone, 7.4 per cent. Drains were not employed solely because of gangrene of the appendix, clear peritoneal fluid, or turbid exudate without odor.

Except in the presence of frank pus, silk was used routinely for removal of the appendix and closure of the abdomen.

The presence or absence, and type, of peritoneal fluid, exudate, or pus in these two groups of cases are shown in Table IV. It is significant and

TABLE IV
INDICATING THE PRESENCE, OR ABSENCE, AND TYPE OF PERITONEAL FLUID
AMONG THE PATIENTS IN BOTH GROUPS
CHARACTER OF PERITONEAL FLUID

Fluid	Per Cent	
	Under 50	Over 50
Clear.....	14.4	7.5
Turbid.....	29.8	15.0
Pus.....	25.4	55.0
Not stated.....	5.3	7.5
None.....	24.9	15.0

typical that actual pus was present in 55 per cent of the patients in the older group. A culture was not indicated, or negative, in 69.2 per cent of the younger patients and 42.5 per cent of the older. As usual in peritonitis of appendiceal origin *Escherichia coli* alone or in combination with other bacteria, was the predominating organism in all positive cultures.

The close similarity in the position of the appendix in these two groups of cases (Table V) is evidence that its location plays no part in the more

TABLE V
LOCATION OF THE APPENDIX DISCLOSED BY OPERATION
LOCATION OF APPENDIX

Position	Per Cent	
	Under 50	Over 50
Right iliac fossa.....	28.5	27.5
Pelvis.....	27.6	27.5
Retrocecal.....	22.4	17.5
Laterocecal.....	6.1	7.5
Retroileal.....	1.3	2.5
Retroileoecal.....	4.4	5.0
Not stated.....	9.6	12.5

fulminating type of disease which frequently occurs in middle-aged and elderly persons. The exactly comparable incidence of appendiceal obstruction by fecolith (Table VI) is of interest, and suggestive of a common factor in the etiology of appendicitis in the two groups.

Since 1925, Maes¹² has stressed the importance of vascular occlusion as the etiologic factor in the rapidly progressive type of appendicitis in patients who have passed the prime of life. In support of this contention, cited by him and others,¹⁶ are replacement of the lymphatic tissue of the appendix by fibrosis as age increases, the terminal nature of its arterial supply, the greater frequency of total rather than localized, patchy gangrene, the higher incidence of thrombosis and pyelophlebitis, and the presence of generalized vascular disease in middle-aged and elderly patients. Gatewood¹⁵ suggests that many cases of appendicitis in older individuals are embolic in origin.

Fitch,⁴ discussing the vascular supply of the appendix, believes that the organ does not atrophy with age but becomes fibrous because of repeated attacks of mild appendicitis, and suggests that circulatory obstruction, when a factor in acute appendicitis, is secondary to distention of the cecum and terminal ileum with fecal material.

It seems quite possible that either of these factors may play a primary rôle in occasional cases of acute appendicitis after the fifth decade of life.

TABLE VI

INCIDENCE AND TYPE OF APPENDICEAL OBSTRUCTION. WHEN NO STATEMENT COULD BE FOUND IN THE OPERATIVE NOTE OR PATHOLOGIC DESCRIPTION RELATIVE TO THE PRESENCE OR ABSENCE OF A FECOLITH, IT IS PROBABLE, THOUGH NOT DEFINITE, THAT NO FECOLITH WAS FOUND.

Obstruction	Per Cent	
	Under 50	Over 50
By fecolith.....	32.4	32.5
By angulation or torsion.....	14.5	5.0
No obstruction.....	10.9	5.0
Not stated.....	36.8	42.5
Appendix not removed.....	5.2	15.0

However, there is available too little accurate pathologic information on the condition of the blood vessels in early cases of acute appendicitis in elderly patients to classify all, or even the majority of cases as primarily vascular in origin. It is the opinion of the writer, based on a study of the operative notes and pathologic reports in this series of cases, that vascular impairment, when present, is, in the large majority of cases, secondary to appendiceal obstruction by fecolith, band, kink, or adhesions.

RESULTS AND MORTALITY

The number of patients, the number of fatalities, and the mortality rate for young and old patients in each of the subdivisions of appendicitis and its complications are summarized in Table VII; the causes of death are listed in Table VIII. If the groups be subdivided less completely, and considered only as patients under and over fifty years of age, with and without perforation of the appendix, the following mortality rates are obtained: One hundred sixty-two patients* less than fifty years old, with no perforation and no mortality; 13 patients over fifty, with no perforations, two fatalities, each due to pulmonary embolism—mortality 15.4 per cent; 66 patients under fifty, with perforation, three deaths due to peritonitis, one

to intestinal obstruction, and one to pulmonary embolism (patient 43 years old)—mortality 7.6 per cent; 27 patients over fifty, with perforation, two deaths due to pulmonary embolism, two to bronchopneumonia, and one to coronary thrombosis—mortality 18.5 per cent.

Although the incidence of perforation with peritonitis or abscess was much higher among the patients over fifty years of age, no death in this

TABLE VII
COMPARATIVE RESULTS OF SURGICAL TREATMENT OF APPENDICITIS AND ITS COMPLICATIONS AMONG
PATIENTS UNDER AND OVER FIFTY YEARS OF AGE

Type of Disease	SUMMARY OF RESULTS Patients Under 50 Years of Age			Patients Over 50 Years of Age		
	Cases	Fatalities	Mortality	Cases	Fatalities	Mortality
Acute appendicitis.....	105	0	0	6	2	33.3%
Ac. ap., with gangrene.....	47	0	0	6	0	0
Ac. ap., with local peritonitis.....	10	0	0	1	0	0
Ac. ap., with perforation and local peritonitis.....	26	1	3.8%	9	2	22.2%
Ac. ap., with perforation and general peritonitis.....	17	3	17.6%	8	2	25.0%
Ac. ap., with abscess.....	23	1	4.3%	10	1	10.0%
Total mortality patients under 50 years of age—				2.1 per cent		
Total mortality patients over 50 years of age—				17.5 per cent		
Total mortality all patients—				4.4 per cent		

group was due to these complications but rather to cardiovascular accidents and pneumonia, degenerative diseases of advancing years, to which old age is heir, regardless of the intervention of acute appendicitis. In the entire series of cases there were only three deaths from peritonitis; these all occurred among the patients who were less than fifty years of age.

The total mortality for the patients under fifty years of age was 2.1 per cent; for patients over fifty years of age it was 17.5 per cent, and for both groups combined it was 4.4 per cent.

TABLE VIII
SUMMARY OF THE CAUSES OF DEATH AMONG THE FATAL CASES IN THE TWO GROUPS OF PATIENTS

Cause of Death	ANALYSIS OF DEATHS	
	Under 50	Over 50
Peritonitis.....	3 patients	0
Intestinal obstruction.....	1 patient	0
Bronchopneumonia.....	0	2 patients
Coronary thrombosis.....	0	1 patient
Pulmonary embolism.....	1 patient	4 patients

CONCLUSIONS

Acute appendicitis is not uncommon after the fifth decade of life in any community or district with a large proportion of its inhabitants over fifty years of age. The disease is often fulminating in character, and may progress to gangrene and perforation with a rapidity equivalent to, or even greater than in adolescence, youth, or early middle life.

The clinical manifestations may be atypical but more commonly vary so little from those which occur earlier in life that a correct diagnosis in most cases should be made without undue delay provided the possibility of appendicitis be kept constantly in mind.

Appendiceal obstruction is responsible for many of the cases of acute appendicitis during the later decades of life; there is very little concrete evidence to support the theory that vascular changes are of initial importance in etiology.

The complications of local peritonitis, general peritonitis, and abscess are much more common among elderly people.

Appendectomy, with or without drainage, should be performed as early as possible after the establishment of a diagnosis, and the institution of pre-operative supportive treatment when indicated.

Middle-aged and elderly persons tolerate peritonitis of appendiceal origin surprisingly well. The mortality in this group, however, is high. Death is frequently due to the hazards of surgery in old age rather than the toxemia of infection, namely, intercurrent pulmonary complications, cardiovascular and cerebral accidents.

REFERENCES

- ¹ DePorte, J. V.: Demography of Otsego County. Rural Medicine, Charles C. Thomas, Springfield, Illinois, 1939.
- ² Walker, Irving J.: A Comparative Mortality Study of Acute Appendicitis. New England J. Med., 208, 113-123, January 19, 1933.
- ³ Ray, Bronson S.: A Study of Appendicitis; 1500 Cases at the New York Hospital. New York State J. Med., 38, 412-423, 1938.
- ⁴ Fitch, Emery M.: Appendicitis in People over Fifty Years of Age. New England J. Med., 198, 348-351, 1928.
- ⁵ Logie, H. B.: Standard Classified Nomenclature of Disease. A. M. A., Chicago, 1937.
- ⁶ Barrow, Woolfolk: Acute Appendicitis in Youth and Old Age. Am. J. Surg., 53, 242-247, August, 1941.
- ⁷ Miller, Edwin M.: Appendicitis in the Aged. S. Clin. North America, 20, 103-108, February, 1940.
- ⁸ Wood, Cornelius B.: Acute Appendicitis in the Aged. Am. J. Surg., 26, 321-325, 1934.
- ⁹ Boyce, Frederick F.: Acute Appendicitis in Middle and Late Life: An Analysis of 421 Cases in Individuals over 39 Years of Age. Am. J. Digest. Dis., 8, 223-230, June, 1941.
- ¹⁰ Lewin, J.: A Clinical Study of Acute Appendicitis in Old Age. Brit. J. Surg., 19, 63-67, 1931-32.
- ¹¹ Stalker, Leonard K.: Appendicitis Among Individuals More Than Sixty Years of Age. Surg., Gynec. & Obst., 71, 54-59, 1940.
- ¹² Maes, Urban: Appendicitis in the Aged. New Orleans M. & S. J., 78, 117-122, 1925.
- ¹³ Maes, Urban, and McFetridge, Elizabeth M.: Acute Appendicitis at the Extremes of Life. South. Surgeon, 4, 422-437, December, 1935.
- ¹⁴ Maes, Urban, Boyce, Frederick, and McFetridge, Elizabeth M.: Acute Appendicitis After Forty. Am. J. Surg., 23, 157-166, 1934.
- ¹⁵ Gatewood, Dr.: Appendicitis in Old Age. S. Clin. North America, 10, 303-307, April, 1930.
- ¹⁶ Miangolarra, C. J.: Age Factors in Acute Appendicitis. New Orleans M. & S. J., 92, 496-498, 1939-1940.

THE PATHOLOGY OF BURNS

THE PATHOLOGIC PICTURE AS REVEALED AT AUTOPSY IN A SERIES OF 61 FATAL CASES TREATED AT THE HOSPITAL FOR SICK CHILDREN, TORONTO, CANADA

I. H. ERB, M.B., ETHEL M. MORGAN, B.S., M.D.,
AND SQUADRON LEADER A. W. FARMER, M.B., M.D.
TORONTO, CANADA

FROM THE DEPARTMENTS OF PATHOLOGY AND SURGERY, HOSPITAL FOR SICK CHILDREN, TORONTO, CANADA

WHILE the pathologic findings in burns have been reported from time to time, the majority of these reports have been of comparatively small numbers of cases. The largest group recently reported is that of Wilson, MacGregor, and Stewart¹ who described the postmortem findings in 33 cases, in 20 of which a study of the clinical course had been made. Whether any of these cases occurred in the period prior to the introduction of tannic acid therapy is not made clear in their article. To supplement the knowledge thus obtained, we are reporting herewith the findings in a larger series of cases than has hitherto been recorded. This series comprises 61 cases of fatal burns occurring over a period of 23 years (1920-1942). During that period the treatment of all burn cases came under the direct supervision of only three clinicians—the late Bruce Robertson, R. I. Harris and, since 1932, one of us (A. W. F.), while the one pathologist (I. H. E.) was responsible for all autopsy records. This has provided an excellent opportunity for the correlation of the pathologic changes with clinical observations, with methods of treatment and with the survival time. The findings are summarized in Table I, and while the clinical observations and methods of treatment have been dealt with more fully elsewhere,^{2*} this article, as the title indicates, has to do chiefly with the pathology. This concerns not only the local skin and adjacent structures, but also such distant organs as lungs, lymph nodes, adrenals, kidneys, liver, and the gastro-intestinal tract. Inasmuch, however, as the changes seem to bear a definite relation to survival time and a possible relation to area burned, and also to treatment, particularly the use of tannic acid, it is proposed to deal with the subject in the light of these factors, perhaps at the expense of some repetition. Since 1928, the surface area burned has been estimated in a manner somewhat similar to that of Berkow's formula.³ Estimations prior to that date were probably less accurate. The nature of the burn (whether fire, scald, chemical, *etc.*) is also recorded in

* Burn Experiences at the Hospital for Sick Children, Toronto, Canada; Farmer, A. W. Read before the American Traumatic Society in June, 1942. To be published in Surgery. In this article the statement was made that liver damage similar to that seen following the use of tannic acid therapy, was seen also prior to its introduction. However, on reexamination of our material, while a certain degree of fatty degeneration of liver is seen in the pretannic acid period, no actual liver necrosis, such as is seen since the introduction of tannic acid, is found.

PATHOLOGY OF BURNS

Table I, but whether a burn is caused by fire or scald appears to bear little relationship to the pathology. Chemical burns in our experience have been too few to venture any opinion as to the existence of any specific pathologic picture.

TABLE I
SUMMARY OF BURN CASES ARRANGED ACCORDING TO SURVIVAL TIME
Survival Time—One Day or Less

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
1 3½ yrs.	Fire 25%	24 hours	Picric acid	Vomiting, convulsions, high temperature.	Congestion of viscera. Few scattered small hemorrhages.
2 4½ yrs.	Fire 30%	24 hours	Picric acid	Primary shock.	Congestion of lungs, adrenals, and kidneys.
3 5 mos.	Scald 3%	12 hours	No local treatment	Acutely ill, cyanosed. Died a few minutes after admission to ward.	Congestion of lungs, liver and kidneys.
4 8 mos.	Scald 25%	24 hours	Borated vaseline	Vomiting, twitchings.	Congestion of viscera. Tiny hemorrhages in lungs.
5 3½ yrs.	Scald 20%	24 hours	Tannic acid	Vomiting, convulsions, high temperature.	Congestion and petechiae of viscera; edema of pleura.
6 2½ yrs.	Scald 35%	9 hours	Transfusion; no local treatment	Shock.	Congestion of viscera. Numerous small alveolar hemorrhages in lung. Leukocytes in periportal areas of liver.
7 6 yrs.	Fire 80%	12 hours	Tannic acid	Comatose and cyanosed.	Congestion of viscera. Small pulmonary hemorrhages.
8 18 mos.	Scald 25%	24 hours	Tannic acid	Mouth burn.	Liver normal on gross examination. No microscopic section examined.
9 18 mos.	Chemical (lysol) 15%	3 hours	No local treatment	Primary shock.	Fatty liver +.
10 4½ yrs.	Fire 85%	3 hours	No local treatment	Peripheral circulation failed.	Congestion of viscera. Small hemorrhages in alveoli
11 2 yrs.	Scald 26%	20 hours	Tannic acid	Vomiting, convulsions.	Congestion of lung and liver. Leukocytes in periportal areas of liver. Small hemorrhages in lung.

Survival Time—Two Days

Case No.	Type and Size of Burn	Survival time	Treatment	Clinical Notes	Pathology Findings
12 2 yrs.	Scald 15%	2 days	Picric acid	Vomiting, convulsions, high temperature, exsanguination transfusion.	Congestion of lungs, liver, spleen, kidneys, adrenals, fatty liver +, postmortem perforation of esophagus.
13 2 yrs.	Scald 20%	36 hours	Sodium bicarbonate	Vomiting, convulsions, high temperature.	Congestion and edema of lungs, congestion of liver, spleen, and kidneys; kidney damage +*.
14 3½ yrs.	Scald 10%	2 days	Tannic acid	Severe hematemesis, high temperature.	Duodenal ulcer with hemorrhage; large adrenal hemorrhage with rupture.
15 5 yrs.	Fire 20%	2 days	Chrome tanning solution	Vomiting, high temperature, toxemia.	Subpericardial and myocardial petechiae; congestion of viscera.
16 22 mos.	Scald 25%	2 days	Tannic acid	Vomiting, convulsions, high temperature—107° F.	Petechial hemorrhages—subpleural, subpericardial, thymus; fatty liver.
17 3½ yrs.	Scald 55%	2 days	Tannic acid	Toxemia.	Cardiac dilatation; congestion and scattered hemorrhages in periadrenal tissues and floor of 4th ventricle.

*The kidney lesions, apart from congestion, consisted of tubular degeneration, the presence of tubular casts and granular precipitate in the glomeruli. For the sake of brevity the kidney lesions are recorded as "kidney damage +, ++, etc." For further details see Table VI.

Survival Time—Two Days

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
18 1½ yrs.	Scald 10%	2 days	Tannic acid	Toxemia, high temperature—108° F.	Congestion of lungs; large thymus.
19 1 yr.	Fire 3%	2 days	Tannic acid	Vomiting, convulsions, high temperature—106°—108° F.	Congestion of lungs, spleen, kidney; slight fat throughout lobules of liver.
20 3 yrs.	Scald 55%	2½ days (60 hrs.)	Tannic acid	Toxemia.	Edema and congestion of lung; early diffuse necrosis of liver; congestion of viscera; small hemorrhage in thymus and mediastinal tissues.

Survival Time—Three Days

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
21 5 yrs.	Scald 20%	3 days	Tannic acid	Toxemia, vomiting; fall of blood pressure.	Congestion and edema of lungs; early aspiration pneumonia; necrosis of liver +++; kidney damage +++; ulcer of esophagus with hemorrhage.
22 10 yrs.	Fire 35%	3 days	Sodium bicarbonate; exsanguination transfusion	Vomiting, delirium, high temperature.	Congestion of lungs and liver; petechiae of myocardium; previous kidney damage (calcified masses).
23 2½ yrs.	Scald 25%	3 days	Tannic acid	Convulsions and collapse.	Liver necrosis +++; pulmonary congestion; subpericardial and peri-adrenal hemorrhages.
24 18 mos.	Fire 25%	3 days	Tannic acid	Vomiting, twitchings, toxemia.	Liver necrosis ++; congestion of meninges, liver, kidney and duodenal mucosa.
25 4 yrs.	Fire 20%	3 days	Tannic acid	Convulsions and twitchings.	Liver necrosis ++; kidney damage ++; pulmonary hemorrhage and edema +.
26 9 yrs.	Fire 20%	3 days	Tannic acid	Toxemia.	Lobular pneumonia; liver necrosis ++++.
27 21 mos.	Scald 10%	3 days	Tannic acid	Toxemia.	Liver necrosis ++; kidney damage ++++; postmortem digestion of stomach.
28 5½ yrs.	Scald 20%	3 days	Tannic acid	Toxemia.	Liver necrosis ++++; early pneumonia; kidney damage ++++; postmortem digestion of stomach.
29 3 days	Scald 10%	3 days (14 hrs. after tan)	Tannic acid	Toxemia ?; drowsy but normal temperature; newborn.	Small hemorrhage in heart and lungs; edema of lungs; cloudy swelling of liver.
30 9 yrs.	Scald 25%	3 days	Tannic acid	Vomiting blood, delirious, coma, toxemia.	Liver necrosis ++++; acute pulmonary edema; hydrothorax, early pneumonia; kidney damage ++++.

Survival Time—Four Days

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
31 5 yrs.	Fire 10%	4 days	Sodium bicarbonate	Vomiting, convulsions, high temperature.	Slight fatty degeneration of liver; congestion of lungs; slight cloudy swelling of kidneys.
32 2½ yrs.	Scald 25%	4 days	Tannic acid	Twitchings, high temperature.	Liver necrosis ++++; kidney damage +; congestion of viscera.
33 2 yrs.	Scald 50%	4 days	Tannic acid	Toxemia.	Liver necrosis ++++; kidney damage ++; congestion of kidneys.
34 2 yrs.	Scald 15%	4 days	Tannic acid	Toxemia, hematocresis.	Liver necrosis ++++; kidney damage ++++; esophageal erosion; extensive pulmonary edema with congestion and alveolar hemorrhage.

PATHOLOGY OF BURNS

Survival Time—Four Days

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
35 6 yrs.	Fire 35%	4 days	Tannic acid	Toxemia.	Liver necrosis + + + +; kidney damage +; jaundice.
36 8 yrs.	Fire 46%	4 days	Tannic acid	Toxemia.	Liver necrosis + + + +; kidney damage + +; congestion of lungs with small hemorrhages.
37 2 yrs.	Scald 20%	4 days	Tannic acid	Vomiting, twitchings, shock, toxemia, jaundice.	Liver necrosis + + + +; kidney damage + +; ascites; hydrothorax; edema of retroperitoneal tissues; jaundice; esophagitis; gastro-intestinal hemorrhage.
38 10 mos.	Scald 10%	4 days	Tannic acid	Vomiting, restless, high temperature, toxemia.	Liver necrosis + + + +; kidney damage + + + +; retropleural and retroperitoneal petechiae — widespread; congestion duodenal mucosa.

Survival Time—Five to Ten Days

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
39 22 mos.	Scald 20%	5 days	Exsanguination transfusion. Tannic acid	Vomiting, drowsy, high temperature.	Central necrosis of liver + + with congestion and hemorrhage; kidney damage +; edema of lung.
40 4½ yrs.	Scald 20%	5 days	Tannic acid; 2 exsanguination transfusions	Vomiting blood, drowsy, coma.	Liver necrosis + + + +; kidney damage + + +; small adrenal hemorrhage; esophagitis.
41 2½ yrs.	Scald 5%	5 days	No local treatment	Admitted with pneumonia; chest scalded by plaster; drowsy; toxic; melena.	Slight fatty liver; extensive bronchopneumonia; duodenal ulcer; cloudy swelling of kidney.
42 1 yr.	Scald 10%	6 days	Soda bicarbonate; borated vaseline	Scarlet fever, vomiting, convulsions, high temperature.	Liver congested; early bronchopneumonia; cloudy swelling of kidney; small adrenal hemorrhages.
43 13 yrs.	Fire 75%	6 days	Tannic acid	Hemolytic streptococcus septicemia.	Liver necrosis +; early bronchopneumonia; cloudy swelling of kidney.
44 6 yrs.	Fire 40%	7 day	Tannic acid; intravenous saline	Hemolytic streptococcus septicemia.	Liver normal; early bronchopneumonia; duodenal ulcer; cloudy swelling of kidney.
45 3½ yrs.	Fire 20%	7 days	Tannic acid	Admitted with whooping cough. Vomiting, twitching, surgical emphysema, high temperature.	Liver necrosis + + +, still hemorrhage in central zones with some polymorphic infiltration; septic pneumonia.
46 2 yrs.	Scald 28%	8 days	Tannic acid	Twitching, labored breathing, sudden collapse.	Liver necrosis—healing stage; kidney damage + +, repair; ulcer of esophagus; pneumonia.
47 4 yrs.	Fire 15%	9 days	Tannic acid	<i>Staphylococcus aureus</i> septicemia.	Liver necrosis—healing stage; pyemic abscesses in myocardium, lungs, kidneys; duodenal ulcer.
48 2½ yrs.	Scald 20%	10 days	Exsanguination transfusion; soda bicarbonate; borated vaseline	Toxemia, high temperature—106° F.	Liver, kidney, adrenals, and inguinal nodes congested.
49 9 yrs.	Scald 25%	10 days	Tannic acid	Burns infected, <i>B. pyocyaneus</i> .	Liver necrosis—healing stage; kidney damage +; adrenal hemorrhage —widespread; duodenal ulcer; early gastric ulcer.

Survival Time—Eleven Days to Three Months

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
50 4 yrs.	Fire 25%	11 days	Tannic acid	<i>Staphylococcus aureus</i> septicemia.	Septic infarct of lung; liver necrosis + +—healing stage; cloudy swelling of kidneys.

Survival Time—Eleven Days to Three Months

Case No.	Type and Size of Burn	Survival Time	Treatment	Clinical Notes	Pathology Findings
51 5 mos.	Fire 2%	12 days	No local treatment	Fried pancakes to chest. Diffuse bronchopneumonia.	Bronchopneumonia; very slight fatty liver in central areas; thrombus in ventricle.
52 2 yrs.	Scald 10%	14 days	Sodium bicarbonate; calcium lactate; exsanguination transfusion	Infected transfusion wound, hemolytic streptococcus.	Liver: Slight fatty infiltration; septic pneumonia.
53 23 mos.	Fire 45%	14 days	Tannic acid; exsanguination; transfusion; excision of burn 3rd day (72 hours)	Profound toxemia, twitchings, drowsy, infected transfusion wounds, sepsis, <i>Staphylococcus aureus</i> .	Liver: fat vacuoles in periportal and middle zones; septic thrombosis femoral vein (transfusion site).
54 4 yrs.	Fire 25%	19 days	Tannic acid	Hemolytic streptococcus sepsis (infected transfusion wound).	Liver necrosis +—repair, mitoses.
55 9 yrs.	Fire 25%	21 days	Soda bicarbonate; picric acid; borated vaseline, 2 transfusions	Severe toxemia early and again last 3 days, with vomiting and high temperature.	Lung: Considerable edema and congestion; small amount cellular exudate. Liver, kidney, mesenteric nodes congested. Axillary nodes edematous.
56 5 yrs.	Scald 5%	21 days	Tannic acid	Hemolytic streptococcus sepsis, scarlet fever, toxemia;	Liver normal; pyemic infarcts in lungs; sepsis.
57 4 mos.	Fire 5%	25 days	Tannic acid	Sepsis, <i>Staphylococcus aureus</i> . Infected interstitial site chest wall.	Liver normal; kidney damage +—repair; medullary hemorrhage of adrenal; <i>Staphylococcus aureus</i> septicemia.
58 2½ yrs.	Scald 20%	5 wks.	Tannic acid	Sepsis, hemolytic streptococcus and <i>B. pyocyaneus</i> .	Diffuse fatty liver +++++; no necrosis; septic pneumonia; thrombosis inferior vena cava and external iliac veins.
59 7 wks.	Chemical Less than 5%	7 wks.	Wet dressings	Child burned at 1 day of age; pneumonia; early malnutrition.	Liver congested, hemosiderin in Kupffer's cells.
60 13 yrs.	Scald 38%	10 wks.	Tannic acid	Septicemia <i>B. pyocyaneus</i> .	Diffuse fatty liver +++++; no necrosis.
61 11 yrs.	Fire 25%	3 mos.	Picric acid	Severe toxemia at first. Postoperative shock (3 hours following skin graft operation).	Liver: Fat vacuoles in periportal zone.

Because of the fact that the pathologic changes seen in burns are most pronounced in those cases dying during the periods of what are commonly called secondary shock and toxemia, some explanation of the use of these terms would seem to be indicated. Elsewhere² we have expressed the opinion that the symptoms of "oligemic anoxia," called also secondary shock, as well as the other symptoms of "toxemia," are the result of absorption of toxins from the area of the burn, and for this reason have included the so-called secondary shock and toxemia under the one heading. This group of signs and symptoms is easily noted in burns of moderate or severe degree. They include briefly: An elevated temperature, rapid pulse, drowsiness, occasionally disturbed by periods of irritability, which drowsiness may go on to coma and death. Often there are localized twitchings and generalized convulsions. Vomiting commences early in severe burns and may become continuous. The limbs become moist and cold. The blood pressure falls eventually. The urine is of small volume, of high specific gravity, and, in

severe cases, may contain albumin, hyalin and granular casts. Acetone may be present.

In the accompanying charts when the term shock is used as indicating the cause of death, this has reference to primary shock as occurring within the first 12 to 24 hours. The term toxemia, on the other hand, includes what is ordinarily spoken of as secondary shock and toxemia. The survival time is indicated in hours, days, weeks, or months. Where the time is expressed in days the figure used indicates the number of complete days of 24 hours plus part of the day on which the patient died. Thus, if a patient survived more than three full days and less than four full days, the survival time is expressed as four days.

The pathologic findings will be discussed under the following headings with emphasis chiefly on gastro-intestinal tract, liver, and kidneys:

1. Skin and adjacent structures
2. Central nervous system
3. Circulatory system
4. Lymph nodes and spleen
5. Respiratory tract
6. Adrenals
7. Gastro-intestinal tract
8. Liver
9. Kidneys
10. Infection

1. *Skin and Adjacent Structures:* It has long been recognized that the size of the burned area in relation to mortality is of more importance than the depth of the burn. Thus, during the period 1913-1941 there was not a single case of recovery when the burned area involved 50 per cent of the body surface and only one case in which 40 per cent of the body surface was burned. Dupuytren's classification of burns according to depth has long been in common use. This has been graphically represented by Harkins.⁴ A somewhat simpler classification is used by the National Research Council of Canada in a recent publication on the Treatment of Thermal Burns.⁵ A comparison of the two classifications is shown in Figure I. The classification referred to in this paper is that of the National Research Council. Briefly, the local changes found in burns of the varying degrees may be summarized as follows:

In burns of first degree there is seen dilatation of the capillaries of the corium and the formation of blisters is a characteristic feature. Fluid collects between the dermis and the overlying damaged epidermis. Should the latter rupture, much oozing of serum follows. This is associated also with edema and leukocytic infiltration of the corium. Burns of the second degree involve not only the epidermis but the dermis, together with varying degrees of damage to the sebaceous and coil glands and hair follicles. The amount of scarring may depend upon the depth of the involvement of the dermis while reepithelization is dependent on the extent to which remnants

of the hair follicles and glandular elements have been spared. In burns of the third degree the whole thickness of the dermis has been destroyed.

2. *Central Nervous System*: Our findings here have been rather meager. In some cases permission to examine the brain was not obtained, and in the majority of those in which examination was carried out only vascular congestion and cerebral edema were found. In one instance petechial hemorrhages were found in the floor of the fourth ventricle (Case 17; survival time

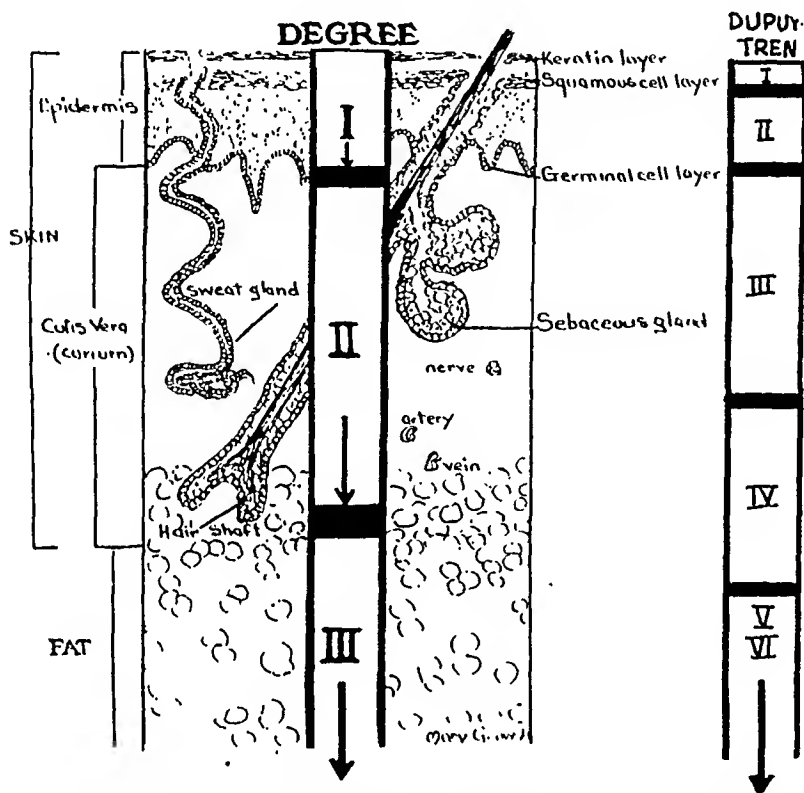


FIG. 1.—Diagrammatic comparison of classification of burns by degrees. Left—according to National Research Council of Canada. Right—according to Dupuytren. Modified from National Research Council of Canada Bulletin 1084.

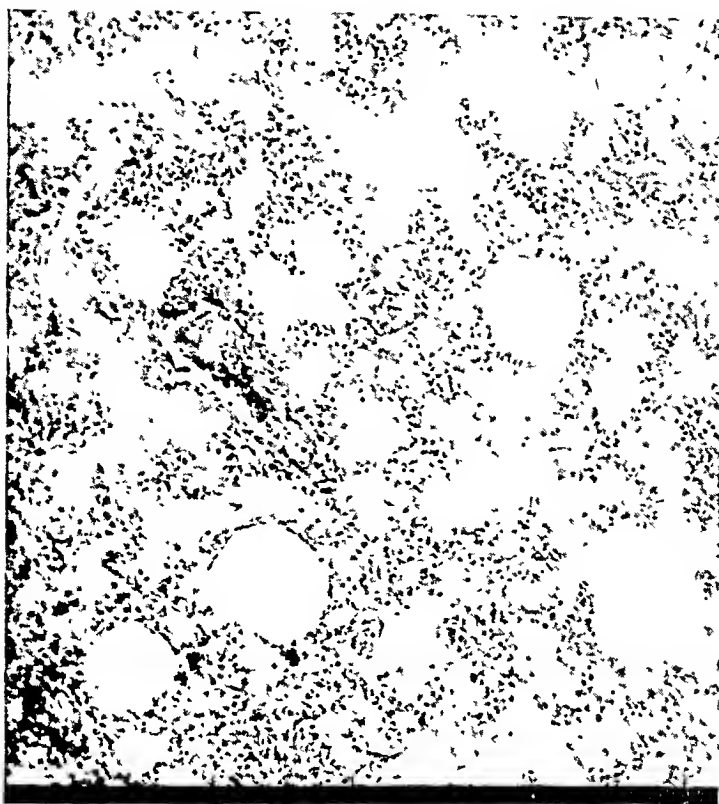
two days). This was associated also with hemorrhages into the periadrenal tissues.

3. *Circulatory System*: Here, again, the changes were slight. In a few instances scattered subepicardial and myocardial petechiae were found, but on no occasion did we see larger hemorrhages, such as have been reported by Harkins⁴ in experimental animals. While, clinically, the symptoms of hemoconcentration appear to be the result of loss of plasma from the circulation, no alterations indicating damage to the vessel walls were observed.

4. *Spleen and Lymphatic System*: Apart from swelling and congestion of vessels, with edema and hemorrhage into the interstitial tissues of the nodes, little of a pathologic nature was noted. In some instances this congestion was very marked.

5. *Respiratory Tract*: During the first 24-hour period, apart from con-

A



B

FIG. 2 A. Case 13: S-T—Two days. Pulmonary edema.
(H. & E., X 80.)
B.—Case 14: S-T—Two days. Massive adrenal hemorrhage.
(H. & E., X 3.)

gestion and petechial hemorrhages, the lungs showed nothing of note. On the second day following the burn, congestion was usually more marked and petechial hemorrhages more pronounced. Edema now appeared in some cases, as shown in Figure 2 A, Case 13. By the third day congestion and edema were still more pronounced, and, should the latter persist, the way may now be paved for the development of a subsequent pneumonia. This complication is dealt with later under the heading "Infection."

6. *Adrenal Glands:* The occurrence of adrenal hemorrhage in burns has

been previously noted.⁶ This lesion was observed in four instances in our series. The survival time in these cases was two, five, six, and 10 days

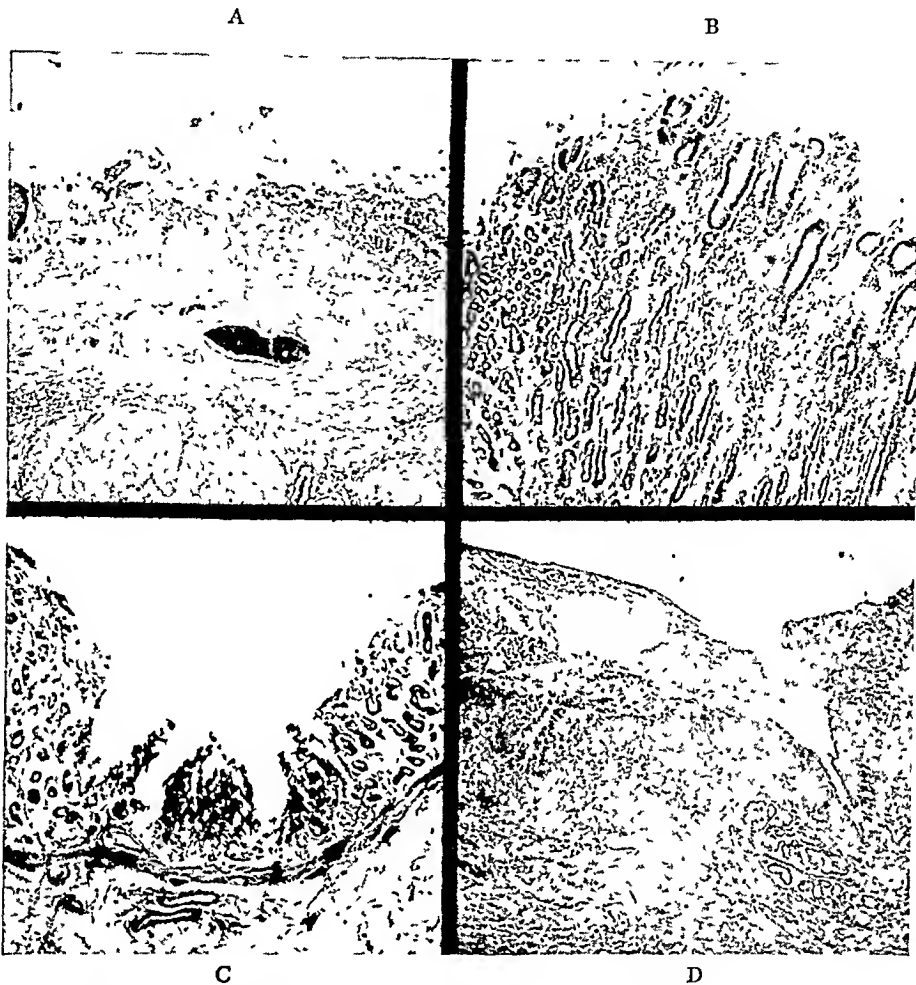


FIG. 3.—Gastro-intestinal Lesions.
A. Case 46: S-T—Eight days. Esophageal ulceration. (H. & E., X 34.)
B. Case 44: S-T—Seven days. Hemorrhage into gastric mucosa, with oozing of blood from mucosal surface. (H. & E., X 48.)
C. Case 49: S-T—Eight days. Early gastric ulcer. (H. & E., X 46.)
D. Case 14: S-T—Two days. Duodenal ulcer. (H. & E., X 34.)

(Cases 14, 40, 42, and 49), respectively. The hemorrhages ranged from quite small medullary ones to more diffuse involvements of the gland, in one instance consisting of an almost spherical mass within the capsule two centimeters in diameter (Fig. 2 B, Case 14; survival time two days).

7. *Gastro-intestinal Tract:* Changes were found in esophagus, stomach and duodenum. In some this consisted only of congestion of the mucosa, while in other cases there was oozing of blood from the congested mucous membrane without definite ulceration. Some of these cases gave a history of vomiting black coffee ground material and in others similar material was found in stomach on postmortem examination. In the esophagus, while varying degrees of superficial erosion were found, in three instances there was ulceration down to the muscularis (Fig. 3 A, Case 46; survival time eight days). The manner in which oozing of blood from gastric mucosa

may occur is illustrated in Figure 3 B. A somewhat more advanced stage of localized epithelial damage is shown in Figure 3 C.

Duodenal ulcers, on the other hand, were found in five cases, or 8.2 per cent, the survival time being 2, 5, 7, 9, and 10 days, respectively. This percentage is somewhat lower than other authors have reported, but, as pointed out by Harkins,⁴ some of these reports are based on collected statistics and not on an individual series as is the case in this paper. The percentage of duodenal ulcers in some reports is, therefore, unduly high. One of these duodenal ulcers occurring in a patient dying on the second day is shown in Figure 3 D. This patient had suffered severe hematemesis (Case 14). In another instance there was found in the base of the ulcer an exposed vessel, which again had given rise to extensive hemorrhage (Case 41; survival time five days).

The cases in which ulceration occurred are summarized in Table II.

TABLE II
GASTRO-INTESTINAL LESIONS
Esophagitis and Esophageal Ulceration

Case No.	Survival Time	Tanned	Remarks
21	3 days	+	Ulceration
34	4 days	+	Ulceration; hematemesis
37	4 days	+	Esophagitis; gastro-intestinal hemorrhage
40	5 days	+	Esophagitis
46	8 days	+	Ulceration
<i>Duodenal Ulcer</i>			
14	2 days	+	Severe hematemesis. Large adrenal hemorrhage
41	5 days	—	Admitted with pneumonia
44	7 days	+	Hemolytic streptococcus septicemia
47	9 days	+	<i>Staphylococcus aureus</i> septicemia
49	10 days	+	<i>B. pyocyaneus</i> infection of burned area; early gastric ulcer, and adrenal hemorrhage

8. *Liver*: Of all the burn changes, those in the liver parenchyma were the most striking. These consisted of first, congestion; then hemorrhage into the central vein areas appeared, accompanied by marked necrosis of the central portion of the liver lobules, involving in some cases two-thirds or more of the lobule. These necrotic changes have been described by Wilson, MacGregor, and Stewart,¹ and Belt.⁷ The most extensive damage was found to occur on the third, fourth, and fifth days. Liver function tests were not carried out on our patients; only two of these cases showed clinical jaundice (Cases 35 and 37). In some of those cases surviving this period, regenerative changes were in evidence.

Because of the possible relationship of tannic acid therapy to liver necrosis, as pointed out by Wells, Humphrey and Coll,⁸ our series of cases will be divided into untanned and tanned groups. Group I (Table III) comprises 20 cases, approximately one-third of the total series, and included 14 cases in the pretannic acid period, from 1920 to 1924, inclusive, and six cases which occurred subsequent to 1924, in which for one reason or another the burned area was not tanned. In Group II are the 41 cases in which tannic acid was used.

TABLE III
TWENTY UNTANNED CASES

Survival Time	Cause of Death			Total
	Shock	Toxemia	Sepsis	
1-24 hours.....	5	2		7
2 days.....		3		3
3-14 days.....		3	4	7
21 days.....		1		1
7 weeks.....			1	1

None showed necrosis of liver. An additional case died of shock following a skin-graft operation, two and one-half months after the burn. Note: Seven of the 20 died in the 3- to 14-day period, when necrosis of liver was a prominent feature in the tanned cases.

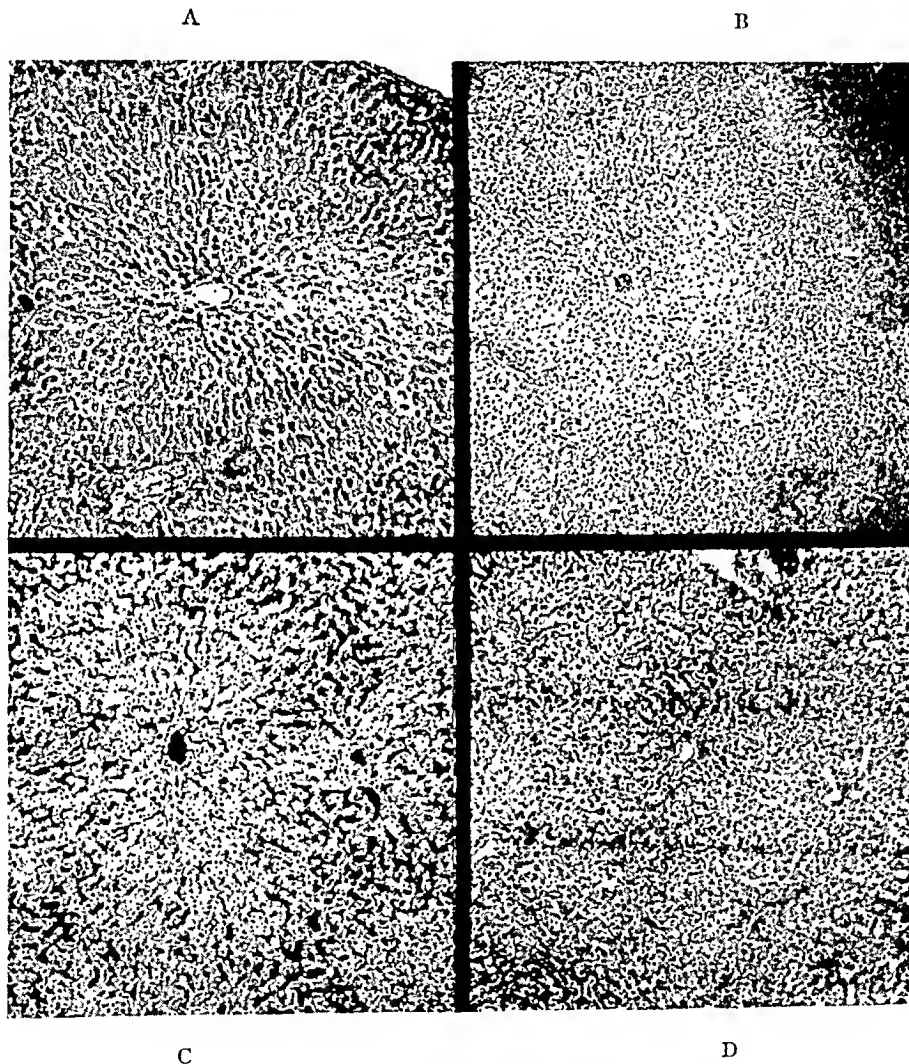


FIG. 4.—Photomicrographs of livers from four untanned cases.
A. Case 22: S-T—Three days. Normal liver. (H. & E., X 51.)
B. Case 41: S-T—Five days. Slight fatty infiltration. No necrosis. (H. & E., X 48.)
C. Case 48: S-T—Ten days. Marked congestion. No necrosis. (H. & E., X 51.)
D. Case 51: S-T—Twelve days. Slight cloudy swelling. No necrosis. (H. & E., X 51.)

The Untanned Group: In the first 24-hour survival-period there were eight deaths, and in these the liver showed no pathologic change apart from varying degrees of congestion. In the survival period from 24 to 48 hours

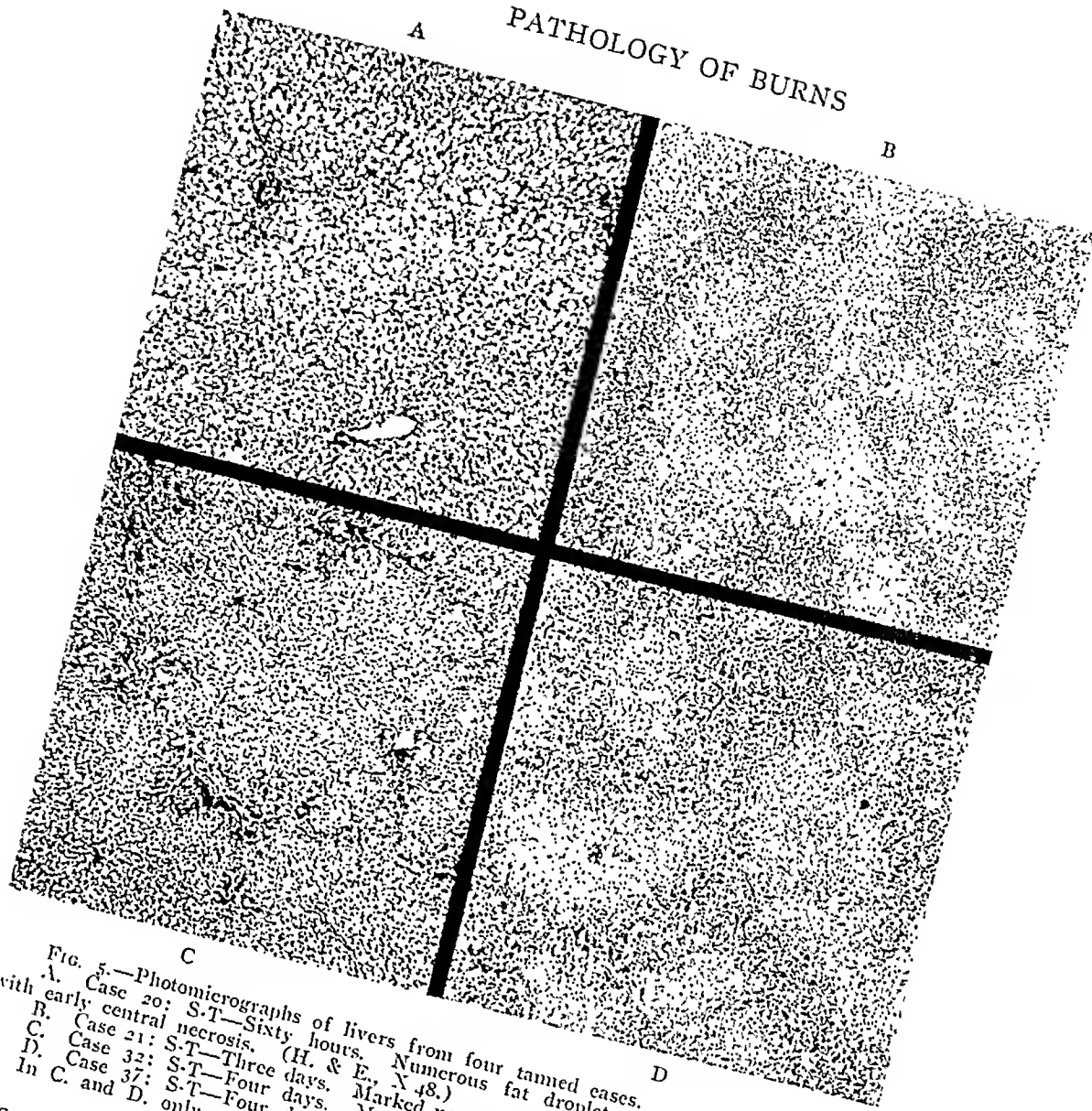


FIG. 5.—Photomicrographs of livers from four tanned cases.
A. Case 20: S.T.—Sixty hours. Numerous fat droplets in periphery of lobule with early central necrosis. (H. & E., X 48.)
B. Case 21: S.T.—Three days. Marked necrosis. (H. & E., X 34.)
C. Case 32: S.T.—Four days. Marked necrosis. (H. & E., X 34.)
D. Case 37: S.T.—Four days. Marked necrosis. (H. & E., X 34.)
In C. and D. only a small fringe of relatively normal cells remains.

there were three cases, one of which showed slight fatty change. In the group in which death occurred from the third to the fourteenth day, inclusive, there were seven cases, four of which showed slight fatty change in the liver cells, but in no instance was there anything approaching necrosis. The microscopic appearance of the livers from four of these cases is shown in Figure 4 A, B, C and D. One patient (Case 59), died in seven weeks of pneumonia and malnutrition, and, apart from some congestion, the liver appeared normal. Another patient (Case 61), died three months after the burn of postoperative shock a few hours following a skin graft operation. The liver in this case showed only some droplets of fat in the cells of the periportal zones.

The Tanned Group: These cases are summarized in Tables IV and V. When we consider these, we find very little difference in the first 24-hour period, in which there were four cases. In the 24- to 48-hour period, there were six cases. Two of these showed no changes of significance. Two

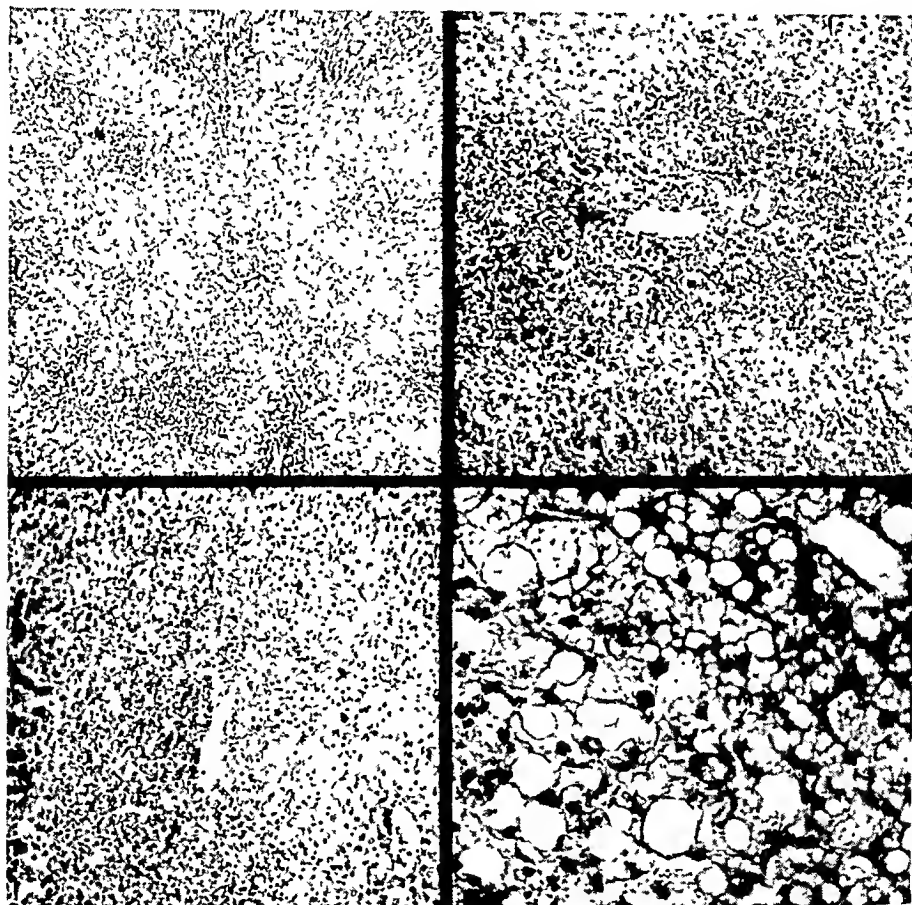
TABLE IV
TWENTY-FIVE TANNED CASES SHOWING LIVER NECROSIS

Survival Time	Liver Necrosis				Cause of Death			Total
	+	++	+++	++++	Shock	Toxemia	Sepsis	
60 hours.....	1					1		1
3 days.....		3	4	1		8		8
4 days.....				7		7		7
5 days.....		1		1		2		2
6-11 days.....	1	4	1				6	6
19 days.....	1						1	1

Note: Seventeen of the 25 died from 3rd to 5th day, inclusive. (See Table VI).

A

B



C

D

FIG. 6.—Photomicrographs of livers from four tanned cases.
A. Case 38: S-T—Four days. Marked necrosis. (H. & E., X 34.)
B. Case 33: S-T—Four days. Marked necrosis. (H. & E., X 80.)
C. Case 36: S-T—Four days. Marked necrosis. (H. & E., X 80.)
D. Case 40: S-T—Five days. More detail of liver damage. (H. & E., X 240.)

showed early fatty degeneration (Cases 16 and 19). One patient (Case 20) died at two and one-half days (60 hours), and showed widespread fatty degeneration, with beginning central necrosis (Fig. 5 A).

In the eight cases dying on the third day, all showed marked necrosis of central and midzonal areas and extending well out into the outer zone (Fig. 5 B). For comparative purposes the degrees of necrosis are indicated in Table IV as two, three, and four plus. In the group dying on the fourth

PATHOLOGY OF BURNS

and fifth days, there were nine cases, eight of which showed marked necrosis, indicated as four plus (Fig. 5 C and D; Fig. 6 A, B, C and D). In the remaining case the damage, while severe, was less marked.

One patient (Case 43) died of hemolytic streptococcus septicemia on the sixth day. This liver showed what we have described as a one plus necrosis.

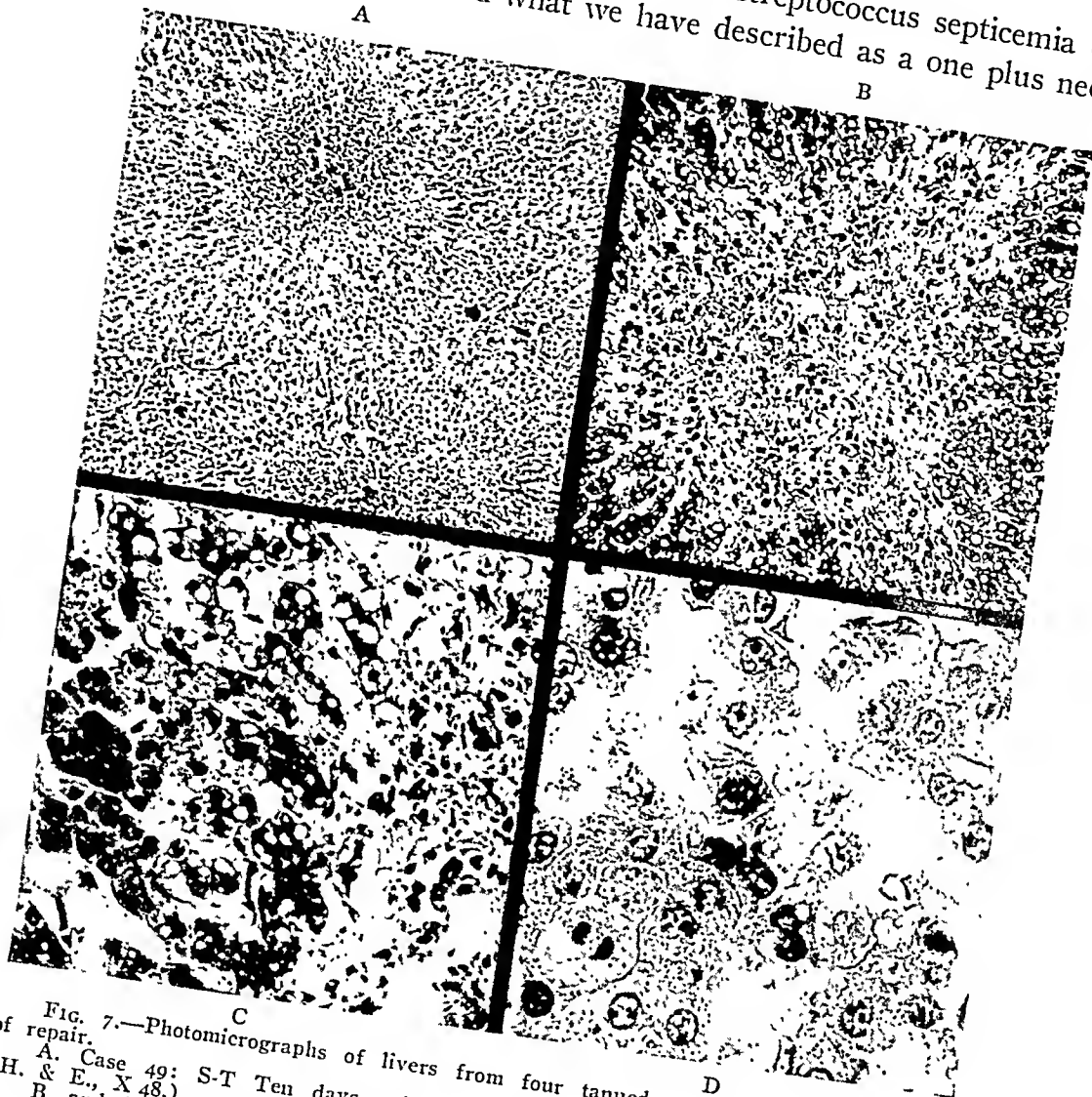


FIG. 7.—Photomicrographs of livers from four tanned cases illustrating process of repair.
A. Case 49: S-T Ten days. Area of necrosis becoming more circumscribed. (H. & E., X 48.)
B. and C. Case 47: S-T—Nine days. Phagocytosis of hemosiderin. (H. & E., X 110 and X 240.)
D. Case 46: S-T—Eight days. Two cells undergoing mitosis. (H. & E., X 510.)

One patient (Case 46) died of pneumonia on the eighth day. Two cases (47 and 49) died on the ninth and tenth days, respectively. These three cases still showed definite central necrosis of liver, but with evidence of healing, in that the necrotic areas were at that time more circumscribed, Kupffer's cells showing phagocytosis of hemosiderin were seen, and in one case mitoses of liver cells (Fig. 7 A, B, C and D).

Of 27 cases dying in the 3- to 19-day period, only three failed to show liver necrosis (Table V). One of these was a newborn infant (Case 29) with a ten per cent burn from a hot water bottle applied at birth; admitted to hospital at two days of age; and tanned only 14 hours prior to death.

TABLE V
SIXTEEN TANNED CASES SHOWING NO LIVER NECROSIS

Survival Time	Cause of Death			Total
	Shock	Toxemia	Sepsis	
1-24 hours.....	2	2		4
2 days.....		5		5
3 days.....		1		1
7 days.....			1	1
14 days.....			1	1
21 days-10 weeks.....			4	4

Details of the three cases dying on 3rd, 7th and 14th days, respectively, are recorded on pages 246 and 248.

Another was the case of a 23-months-old infant (Case 53), with a 45 per cent fire burn, tanned within six hours of admission. By the third day toxemia had become so profound that an attempt was made to halt its further development by excising the greater part of the burned and tanned area. Its condition improved for a time, but later a transfusion wound became infected and the child died of sepsis on the fourteenth day. The liver showed only slight fatty change (Fig. 8). The third of these cases

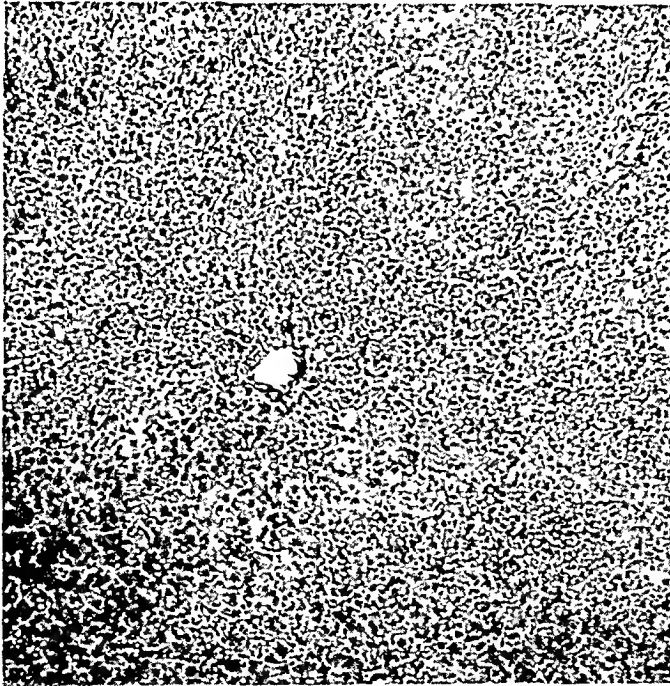


FIG. 8.—Case 53: S-T—Fourteen days. Photomicrograph of liver showing slight fatty change. Burned and tanned area excised on third day. (H. & E., X 51.)

(Case 44) showing no necrosis, was that of a six-year-old girl, with a 40 per cent fire burn (Fig. 9); tanned on admission; and dying on the seventh day, with hemolytic streptococcus septicemia. No gross or pathologic liver changes could be found (Fig. 10). She did, however, have a duodenal ulcer. While she received abundant intravenous saline, she had no glucose solution administered.

The survival times in the *tanned and untanned* groups are compared in Figure 11. Thus, it is seen that in the untanned group 35 per cent of

deaths occurred within the first 24 hours, while in the tanned group 53 per cent died in the three- to seven-day period. In other words, with the introduction of tannic acid, the average survival time has shifted from the period of primary shock to that of toxemia.

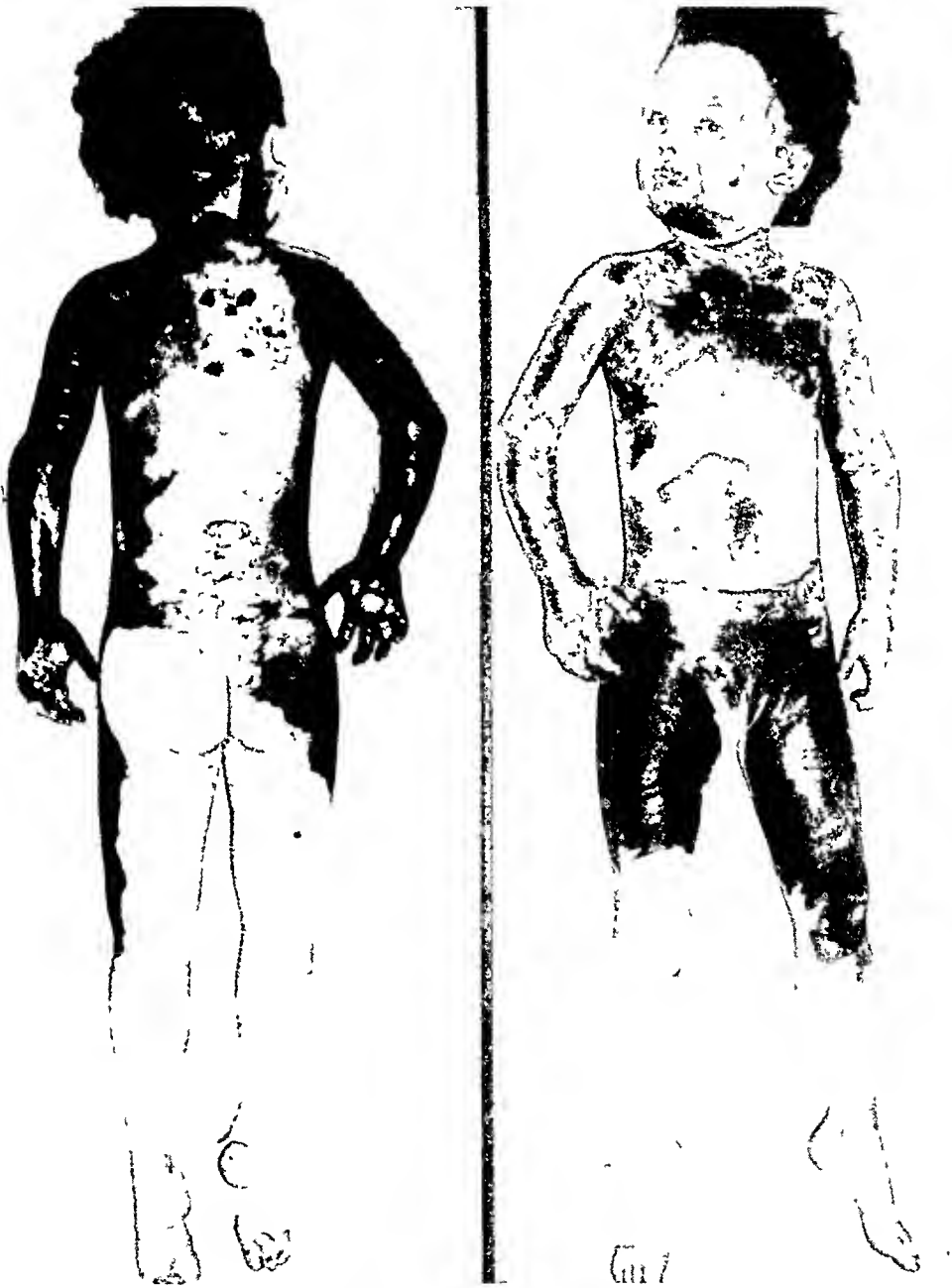


FIG. 9.—Case 44: S-T—Seven days. Burned and tanned area. Death from streptococcus infection.

9. *Kidneys*: The lesions in kidney involved both tubules and glomeruli. The tubular changes consisted of varying degrees of epithelial degeneration, from slight to very severe, with destruction also of many of the nuclei and the presence of numerous droplets of fat in the remaining cytoplasm, particularly towards the basement membrane. In the majority of cases showing epithelial damage, were seen also hyaline and finely granular

casts in both convoluted and collecting tubules, particularly the latter (Fig. 12 A, B, C and D).

Apart from varying degrees of congestion, particularly in those cases dying within the first 24 or 48 hours, the glomerular lesion consisted of deposits of a granular precipitate in the glomerular space (Fig. 13 A, B, and C). The extent to which this was seen is indicated by one or more plus signs in the accompanying Table VI.

TABLE VI
KIDNEY DAMAGE

Survival Time	+	++	+++	++++	Total
36 hours.....	1*				1
3 days.....	1	1	2	1	5
4 days.....	2	3		2	7
5 days.....	1		1		2
8-10 days.....	1	1†			2
25 days.....	1‡				1
70 days.....	1				1

Note: Fourteen of the 19 cases died from the 3rd to 5th day, inclusive. (See Table IV.)

*The only untanned case.

†Showed repair.

‡Complicated by miliary abscesses.

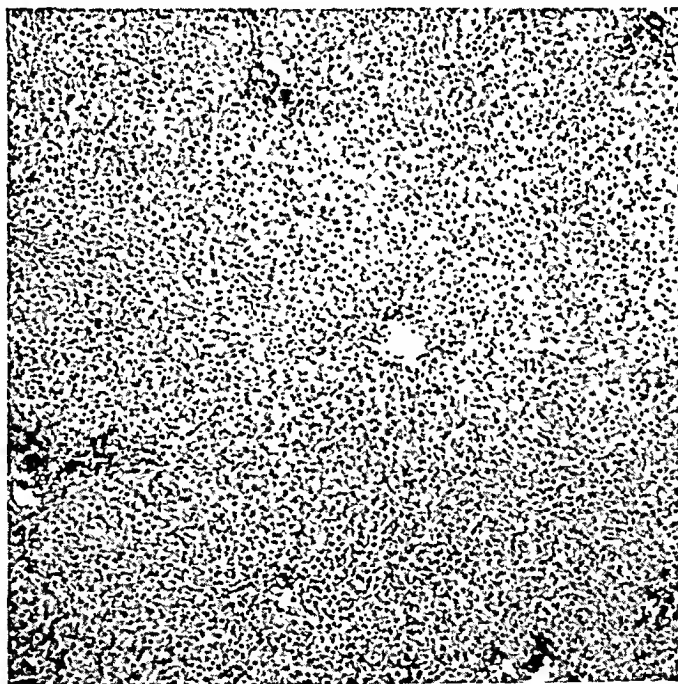


FIG. 10.—Case 44: S-T—Seven days. (See Fig. 9.) Photomicrograph of liver. No necrosis. (H. & E. $\times 48$).

One interesting feature is revealed in the study of the kidney in Case 46, dying on the eighth day. In this case there was no glomerular precipitate. Casts were relatively few and the degenerative changes in the tubular epithelium had altered. While many of the tubules were still dilated and while there was still some débris in the lumina, the majority of the epithelial cells appeared now to have an intact cell membrane. Here and there were scattered epithelial cells undergoing mitoses (Fig. 13 D). These changes

PATHOLOGY OF BURNS

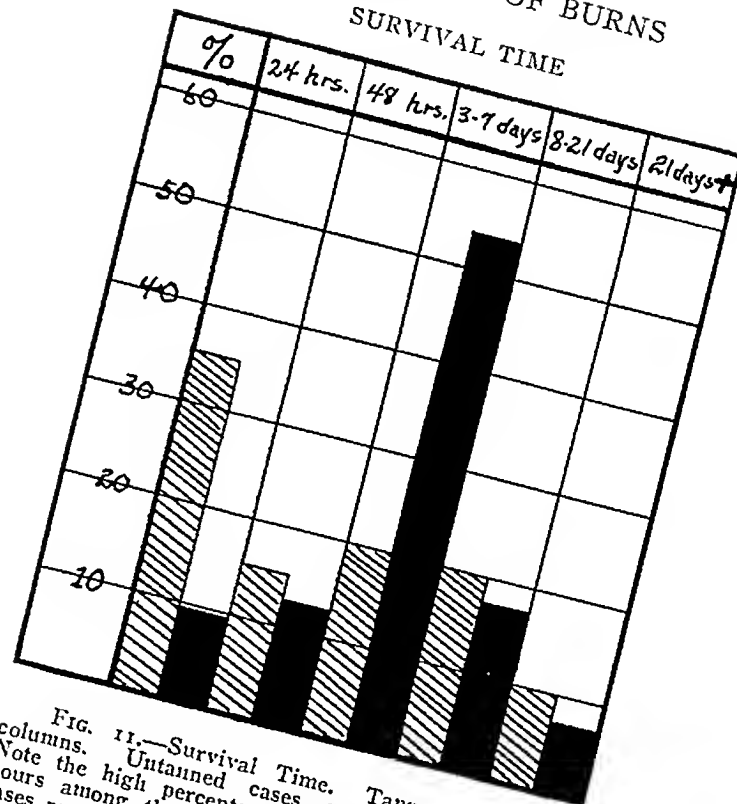


FIG. 11.—Survival Time. Untanned cases cross-hatched columns. Note the high percentage of deaths in the first 24 hours among the untanned cases, while the tanned cases reach their maximum from 3rd to 7th day.

are interpreted as evidence of repair. Interestingly enough, this case, which best illustrates repair in the kidney, also shows definite evidence of repair in the liver (Fig. 7 D).

Changes of one degree or another, involving either tubules or glomeruli, were found in 18 of the 61 cases. In only one of these (Case 13, survival time 36 hours) was tannic acid not used, and in this instance the glomerular precipitate was not marked. Neither tubular degeneration nor casts were found.

In Case 57, survival time 25 days, the renal picture was complicated by military abscesses, death having resulted from *Staphylococcus aureus* septicemia. Also, in Case 60, survival time 10 weeks, in which death resulted from sepsis with *B. pyocyaneus* infection, the changes were slight. Of the remaining 15 cases, survival time varied from three to ten days, with 13

TABLE VII
INFECTION AS A CAUSE OF DEATH

Lesion	Survival Time in Days				Total
	3	5-7	9-14	19-70	
Pneumonia on admission.....	2	1	1		2
Developed pneumonia.....		1			2
Whooping cough on admission.....		1			1
Scarlet fever.....		1			2
Sepsis from burned area.....		2	3	1	6
Transfusion wound.....			2	1	4
Interstitial wound.....				1	1

Note: 31 per cent of tanned cases infected.
25 per cent of untanned cases infected.

dying on the third to fifth day. Reference to Table I reveals the fact that everyone of the 15 cases with kidney changes in which there was a survival time of three to ten days, showed also necrosis of the liver. This suggests, at least, that the same noxious agent is responsible for both kidney and liver damage.

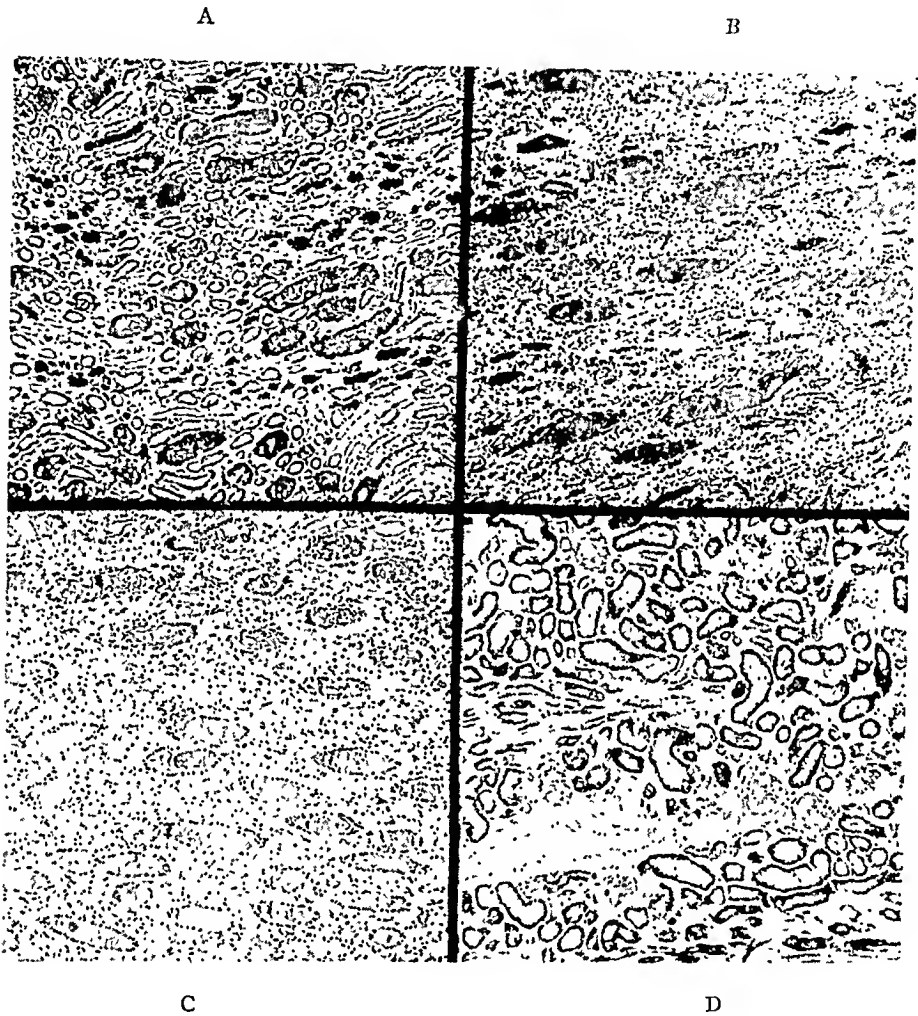


FIG. 12.—Kidney Lesions. A, B, and C, photomicrographs from three cases showing numerous casts in collecting tubules.

- A. Case 30: S-T—Three days. (H. & E., X 51.)
- B. Case 21: S-T—Three days. (H. & E., X 51.)
- C. Case 38: S-T—Four days. (H. & E., X 51.)
- D. Showing tubular degeneration with extensive deposits of fat (black) in epithelial cells. Same Case as C. Scarlet red stain. (X 48.)

10. *Infection:* Under the heading "Infection as a Cause of Death" are included 18 cases (Table VII). Of these, two were admitted with pneumonia, the burns having been sustained as the result of injudicious application of a hot plaster in one instance and of hot pancakes in another. One patient was admitted with whooping cough; developed pneumonia; which was complicated by surgical emphysema. Two patients died of scarlet fever, one of which was admitted during the incubation period. Two patients died on the third day, with early pneumonia, in both of which the primary infection appeared to be in the respiratory tract. In six cases

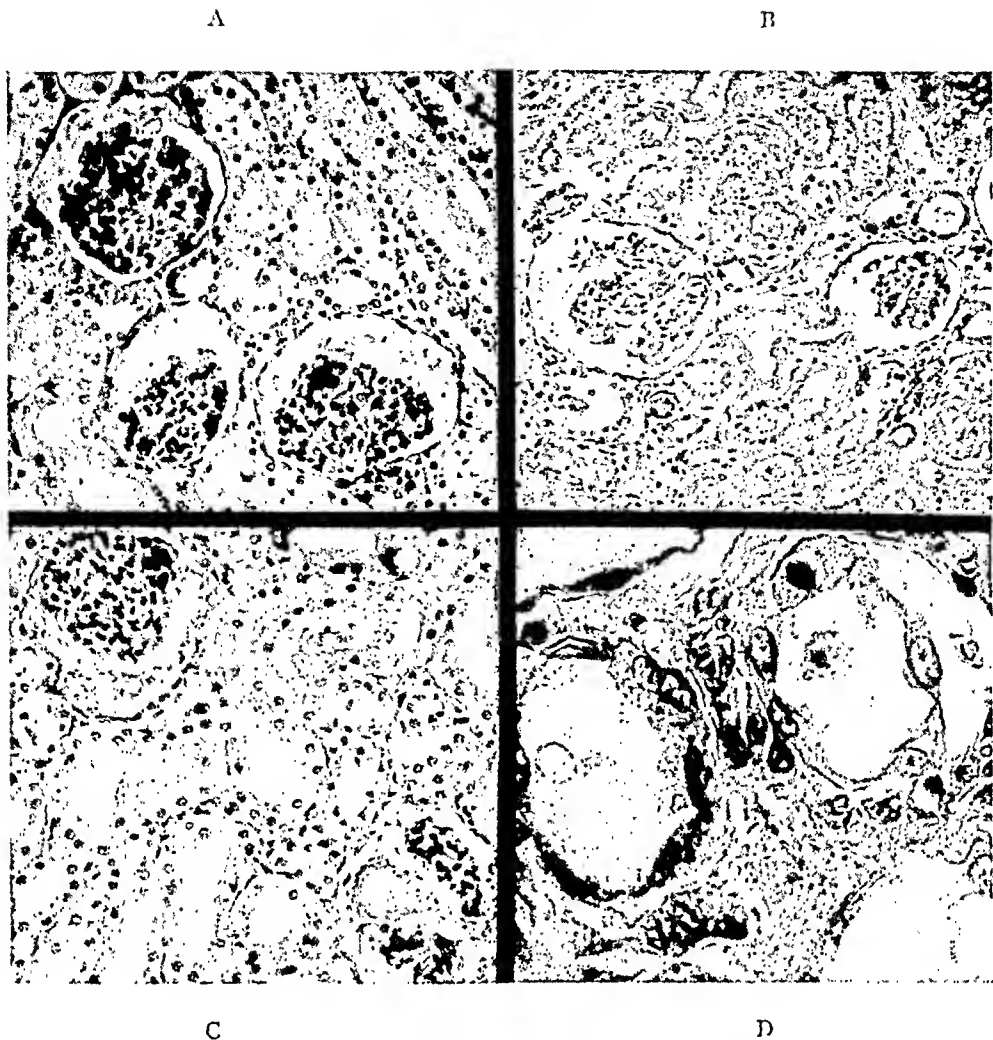


FIG. 13.—Kidney Lesion. A, B, and C, photomicrographs from three cases showing debris in glomerular space; also epithelial damage, particularly in B.
A. Case 27: S-T—Three days. (H. & E., X 160.)
B. Case 34: S-T—Four days. (H. & E., X 120.)
C. Case 40: S-T—Five days. (H. & E., X 160.)
D. Case 46: S-T—Eight days. Tubular repair. One mitotic figure. (H. & E., X 510.)

with septicemia the source of the infection appeared to be in the burned area. In four, transfusion wounds became infected, and in one, infection started at the site of an interstitial saline injection in the chest wall. Ten of these 11 cases were tanned. The invading organism in those cases in which it was identified was as follows: Hemolytic streptococcus, five, *Staphylococcus aureus*, four, *B. pyocyaneus*, two, hemolytic streptococcus combined with *B. pyocyaneus*, one, *B. influenzae* combined with pneumococcus Type X, one.

In Table VIII are shown the burn mortality rates at the Hospital for Sick Children over a period of 28 years. Following the introduction of

TABLE VIII
MORTALITY RATES
Treatment

Period	Mortality Rate
1913-1924	Prior to tannic acid 35.2%
1925-1928	Tannic acid and exsanguination transfusion 16.1%
1929-1937	Tannic acid 11.8%
1938-1941	Tannic acid, Sulphonamides plus plasma, and other measures 2.9%

Note: It is understood that additional therapeutic measures were also taken in all these periods.

tannic acid in 1925, the rate fell from 35.5 to 16.1 per cent, and, again, in the period from 1929-1937 to 11.8 per cent. In the four-year period, 1938-1941, there was a further drop to 2.9 per cent, which has been attributed to the introduction of the sulpha drugs, intravenous plasma, cortin and other measures. The details of therapy are discussed elsewhere.²

SUMMARY

1. The postmortem findings in 61 fatal cases of burns are reported. Of these, 41 were tanned with tannic acid and 20 were untanned.

The more important changes remote from the burned area, and apparently of a toxic origin, involve liver, kidney, gastro-intestinal tract and adrenal, while infection of one sort or another takes its added toll. In the gastro-intestinal tract, duodenal ulcer was observed five times, one of which cases was untanned. Esophagitis or esophageal ulceration was observed in five cases, all of which were tanned. Early gastric ulcer, or oozing of blood from gastric mucosa without ulceration, was observed three times. Adrenal hemorrhage occurred four times, in three of which cases the patient was tanned. Renal damage was shown in the form of precipitate in the glomerular space or tubular degeneration and casts. Most of these occurred from the third to the fifth day inclusive. Signs of repair were noted after the eighth day.

2. Of 41 cases in the tanned group, 25, or 61 per cent, showed liver necrosis.

3. The shortest survival time in which necrosis was found was 60 hours, the longest was 19 days.

4. Of the 25 patients showing necrosis, one died in 60 hours, 17 died in the period of three to five days, inclusive, seven died in the period six to 19 days, inclusive.

5. The degree of necrosis was graded as follows: + + + +, nine cases; + + +, five cases; + +, eight cases, and +, three cases.

6. Death up to the fifth day was attributed to toxemia. Death from the sixth day on was due, in part at least, to infection of one sort or another.

7. Signs of repair of liver were noted in each of five cases, in which death occurred from the eighth to the nineteenth day.

8. Of 27 tanned cases dying in the three- to 19-day period, only three failed to show liver necrosis. One of these was tanned only 14 hours prior to death, and in another the burned and tanned area had been excised on the third day in an attempt to halt the rapidly increasing toxemia. (The child died of sepsis on the fourteenth day).

9. No case of liver necrosis occurred in the untanned group, seven of which died in the three- to 14-day period, in which necrosis was an outstanding feature in the tanned group.

10. Kidney damage was observed in 19 cases, all but one of which belonged to the tanned group.

On the other hand, it should be pointed out:

(1) Following the introduction of tannic acid in 1925, the mortality rate from burns fell from 35.2 to 11.8 per cent prior to the use of sulfanilamides, and to 2.9 per cent since their introduction, along with other measures.

(2) Also following the introduction of tannic acid the time at which death usually occurs has shifted from the early period (first 12-36 hours) into the period of toxemia (third to sixth day), a period in which liver necrosis is most frequently observed.

(3) The patients dying *with* liver necrosis, apart from those dying of sepsis, presented, on the whole, the same clinical picture of toxemia as did those without liver necrosis who were untanned and died in the same period.

(4) The liver necrosis, therefore, whatever its cause, is not necessarily the cause of death, although it may be a serious complication.

(5) It has been shown that this necrosis of liver may undergo repair.

(6) The survival for seven days of one patient with 40 per cent burn, tanned within six hours, and showing at autopsy a normal liver, may point the way to a search for some therapeutic agent to be used in combination with tannic acid, by which the benefits of tannic acid may be preserved and by which, at the same time, the liver may be protected from necrosis, be that necrosis the result of absorption of a toxic substance from the burned skin, the direct or indirect result of tannic acid, or a combination of both.

REFERENCES

- ¹ Wilson, W. C., MacGregor, A. R., and Stewart, C. P.: Clinical Course and Pathology of Burns and Scalds under Modern Methods of Treatment. *British Jour. of Surgery*, 25, 826, 1938
- ² Farmer, A. W.: Burn Experience at the Hospital for Sick Children. Read in Boston before the American Association for the Surgery of Trauma, June, 1942. To be published.
- ³ Berkow, S. G.: Method of Estimating Extensiveness of Lesions (Burns and Scalds) Based on Surface Area Proportions. *Arch. Surg.*, 8, 138, 1924.
- ⁴ Harkins, H. N.: The Treatment of Burns. Springfield, Ill., Thomas, 1942.
- ⁵ Treatment of Thermal Burns. Bulletin No. 1084, National Research Council of Canada, Ottawa, August, 1942.
- ⁶ Snelling, C. E., and Erb, I. H.: Hemorrhage and Subsequent Calcification of the Suprarenal. *Jour. of Pediatrics*, 6, 22, 1935
- ⁷ Belt, T. H.: Liver Necrosis Following Burns, Simulating the Lesions of Yellow Fever. *Jour. of Path. and Bact.*, 48, 493, 1939
- ⁸ Wells, Humphrey, and Coll: Relation of Tannic Acid to the Liver Necrosis Occurring in Burns. *New Eng. Jour. of Med.*, 226, 629, 1942.

THE INTRA-ABDOMINAL USE OF THE MIKULICZ PACK

THOMAS E. JONES, M.D., JOHN R. PAXTON, M.D.,
AND ROBERT E. BRUBAKER, M.D.

CLEVELAND CLINIC
CLEVELAND, OHIO

THE ABDOMINAL SURGEON is frequently confronted with the problem of dealing with large surfaces which cannot be reperitonealized or covered with omentum after extensive dissections of adherent masses. In regional enteritis, for example, he may be forced to resect a fixed mass involving several feet of small intestine and perhaps a portion of the ascending colon, rendering the entire right lower abdomen a raw, oozing surface. After mobilization of a large neoplasm of the sigmoid, the major portion of the pelvic basin may be denuded of peritoneum.

We have been impressed in these and similar instances with the value of the mechanical exclusion of the small intestines from contact with such areas. If loops of small bowel are allowed to prolapse into a freshly denuded intra-abdominal basin, some degree of obstruction frequently occurs, due to adherence and kinking. In addition, if such an area is infected or contaminated, at least a localized peritonitis will result. The abdomen can withstand peritoneal infection to a marked degree, but the combination of infection and obstruction may frequently be fatal. A mechanical barrier which will cover the unperitonealized surface and fill the space from which a mass has been removed will prevent such an occurrence.

Mikulicz,¹ in 1886, suggested the use of a gauze pack for walling-off large unperitonealized areas after extensive pelvic operations. Little attention was given the "Mikulicz pack," as it was subsequently named, until Faure^{2, 3, 4} reintroduced it into France in 1921. Since then, many publications have appeared in the continental literature describing modifications in the technic and extensions of its application. Only a few articles have appeared in the English literature, and we believe the value of this contribution of Mikulicz' may well be restated.

The original Mikulicz pack consisted of a mesh sac, packed with strips of gauze, which was placed into the denuded pelvic basin. The gauze strips were removed gradually, and finally the surrounding mesh sac, leaving a granulating cavity. Faure employed the pack in its original form at the conclusion of the radical Wertheim operation. Following his work, numerous reports appeared, particularly in the French and Italian literature. Descio,⁵ Cosma,⁶ Patti,⁷ Salvini,⁸ Dogliotto,⁹ Alphonse,¹⁰ Rouhier,¹¹ Andre,¹² Villard,¹³ Audain,¹⁴ Chaton,¹⁵ Sabadini,^{16, 17} Dambin and Thomas,¹⁸ Leclercle,¹⁹ Lazarides,²⁰ Perrin,²¹ Keller,²² Massabrau,²³ Lascaux,²⁴ Rousseaux,²⁵ Alcorto,²⁶ Grigoriu,²⁷ Andrien,²⁸ Panchett,²⁹ Berger,³⁰ Cadenet,³¹ and Corachan and Armangue,³² discussed the subsequent uses of the pack and its modifications.

The mesh sac of the original pack was replaced by gutta-percha which

had the advantage of easy removal. The indications for the gutta-percha pack were extended widely, and it was used not only to exclude the small intestines from unperitonealized areas, but also to present their prolapse into abscess cavities. Gibson,³³ in 1921, suggested the use of the modified pack in acute appendicitis. Farr³⁴ reported 162 cases, and Weeden³⁵ 455 cases

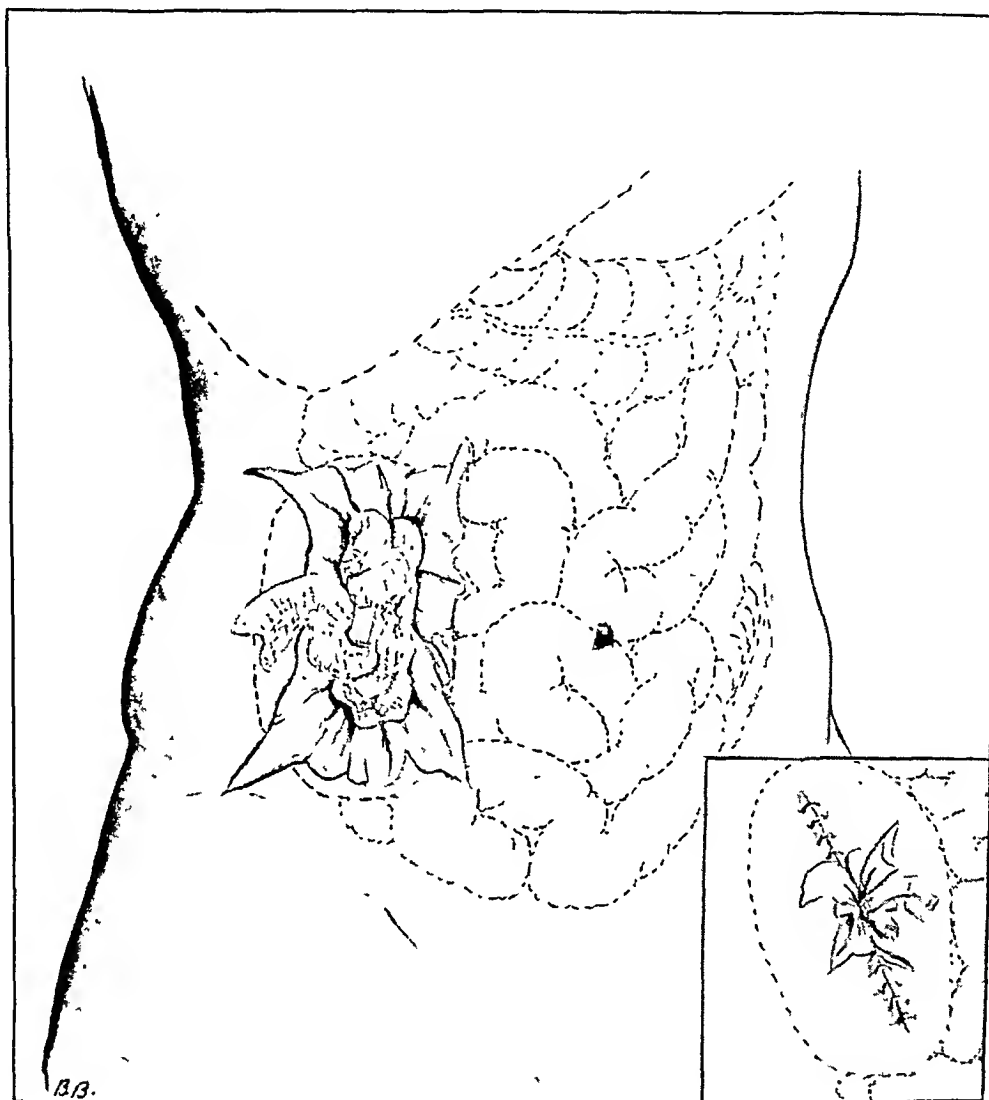


FIG. 1.—Diagrammatic sketch of pack after closure.

using the Gibson technic. Price described the “coffer dam” which may be considered a modification of the Mikulicz pack. Kennedy,³⁶ a pupil and staunch supporter of Price, practices the principle extensively. Coffey,³⁷ in 1937, reported a modification using gauze wicks surrounded with rubber dam, and gave a comprehensive review of its application as a mechanical barrier and as a drain. He termed this pack an “abdominal quarantine” which is an apt phrase for the principle.

TECHNIC

For many years the senior author has used a modification of the Mikulicz pack, employing a sheet of rubber dam into which a large fold of gauze

is packed. This may be applied in two ways, depending upon the size and shape of the area to be covered: (1) A large square sheet of rubber dam is placed against an unperitonealized area and packed with a long gauze fold until the cavity formed by the removal of a mass is filled with the

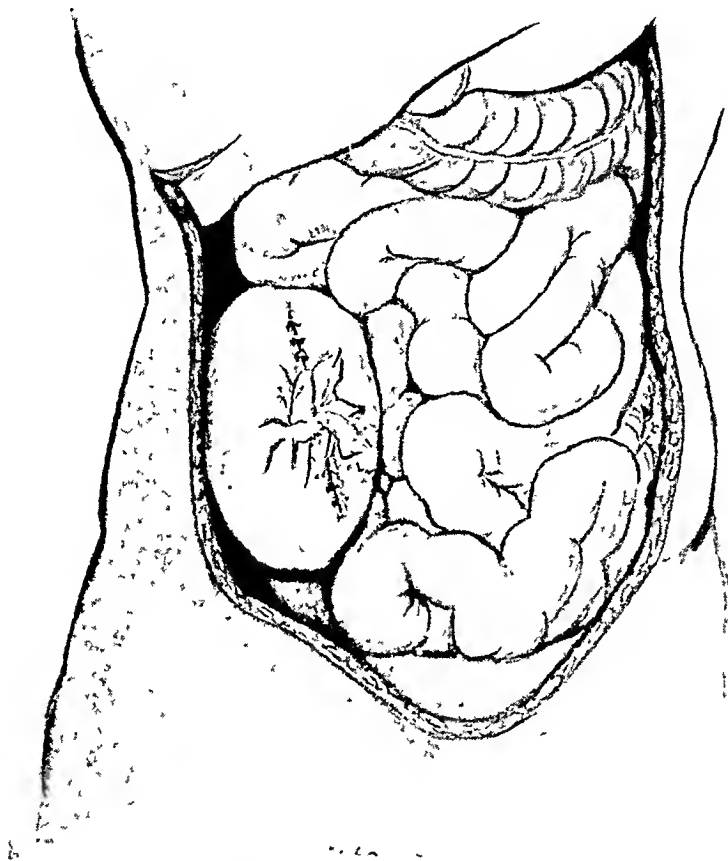


FIG. 2.—Diagrammatic sketch of pack intra-abdominally.

bulk of the pack (Fig. 1). The four edges of the rubber dam square are then gathered together and are brought out of the abdominal wound together with the inner gauze fold (Fig. 1 A). The pack assumes a sac-like shape with the neck at the abdominal wall (Fig. 2). One need not be concerned about the formation of a large intra-abdominal cavity with a relatively narrow opening, since it collapses rapidly within a few days after the entire pack is removed. (2) In the case of a deep, narrow, unperitonealized area, one edge of a rectangular piece of rubber dam is placed into the bottom of the area and folded over gauze packing, forming in appearance a large cigarette drain.

In each case the inner gauze packing is removed gradually beginning the third or fourth postoperative day. The last portion of the pack and the rubber dam are usually removed between the eighth and the eleventh postoperative day. A large rubber tube or catheter is placed into the cavity formed by the pack, and irrigations are carried out as often as necessary

USE OF MIKULICZ PACK

until it closes. With careful postoperative attention such cavities assume the shape of vertical sinuses within a week, and the wounds are entirely healed in six to ten weeks.

USES

We have found this type of pack of greatest value in two groups of cases: First, regional enteritis, especially those cases with enterocutaneous fistulae; and second, neoplasms of the sigmoid colon and the splenic and hepatic flexures.

In regional enteritis with fistula formation, one nearly always finds at operation a densely adherent mass formed by loops of small intestine and often by the ascending colon. Extensive mobilization is necessary, leaving a large raw surface in the right lower abdomen. Furthermore, some degree of contamination is almost unavoidable in the dissection of the sinus tracts. In these cases we believe that the use of the modified Mikulicz pack leads to a smooth convalescence and frequently prevents a mortality which otherwise might be expected.

Neoplasms of the splenic flexure are the bane of surgery of the colon. Mobilization of the lesion is frequently difficult, and a wide area of peritoneum is denuded high in the upper left colonic gutter. It is hazardous to allow the small intestines to prolapse into the cavity formed by the dissection. In such instances, where reperitonealization is impossible, a Mikulicz pack is used routinely to fill this space. The pack is brought out through a stab incision in the left flank. With neoplasms of the hepatic flexure, the same situation frequently exists.

Large, bulky, adherent carcinomata of the sigmoid colon often present difficulties. Frequently, they are surrounded by marked pericolic inflammation and abscesses. Mikulicz pack is the answer to the problem of handling the denuded and infected surface.

The following are typical examples from a series of over 75 cases in which the pack has been used:

ILLUSTRATIVE CASES

Case 1.—Mr. A. M., age 38. *Diagnosis:* Regional enteritis with enterocutaneous fistula. *Operation:* Ileotransverse colostomy and resection terminal ileum and ascending colon in two stages. Resection of adherent mass right lower abdomen involving ileum and ascending colon. About ten feet of bowel resected. Sinus tracts destroyed with cautery. Large denuded area covered with rubber dam pack. *Course:* Uneventful. Entire pack removed by 8th day. Small sinus tract at end of four weeks. Wound healed in six weeks.

Case 2.—Mr. S. L., age 22. *Diagnosis:* Regional enteritis with enterocutaneous fistula. *Operation:* Ileotransverse colostomy and resection terminal ileum and ascending colon. Two-stage operation. Large mass right lower abdomen involving loops of ileum and ascending colon. Six to eight feet of bowel resected. Large unperitonealized area covered with rubber dam pack. *Course:* Uneventful. Entire pack removed 12th day. Sinus closed in eight weeks.

Case 3.—Mrs. B. F., age 56. *Diagnosis:* Carcinoma of splenic flexure. *Operation:*

(1) Preliminary cecostomy. (2) Resection of carcinoma of the splenic flexure. Splenectomy. Large mass bound down to posterior and lateral abdominal walls and to splenic vessels. Separated from lateral wall by blunt dissection. In separation from splenic vessels, hemorrhage occurred necessitating splenectomy. Dissecting posteriorly, abscess was encountered. Mikulicz pack was inserted into hollow produced by splenectomy and removal of mass. *Course:* Dam removed on 8th day. Wound entirely healed in six to eight weeks.

Case 4.—Mr. L. P., age 50. *Diagnosis:* Carcinoma splenic flexure. *Operation:* Mikulicz resection. Neoplasm splenic flexure, adherent to parietal peritoneum and to spleen. Large denuded area high in left colonic gutter filled with Mikulicz pack brought out through stab incision in left flank. *Course:* Uneventful. Pack removed 11th day. Sinus healed in six weeks.

Case 5.—Mr. E. L., age 59. *Diagnosis:* Carcinoma of the sigmoid. *Operation:* (1) Preliminary cecostomy. (2) Anterior resection of the sigmoid. Large mass three inches above peritoneal reflection, diffusely adherent to posterior surface of bladder and to posterior abdominal wall. Peritoneal floor only partially reconstructed. Mikulicz dam inserted into large unperitonealized area. *Course:* Packing began to be removed on 5th day. Dam removed on 10th day. Sinus healed in four weeks.

Case 6.—Mrs. M. B., age 50. *Diagnosis:* Carcinoma of descending colon. *Operation:* (1) Preliminary cecostomy. (2) Anterior resection descending colon. Large mass six inches above peritoneal reflection, firmly fixed to posterior abdominal wall. In freeing mass, fracture of the growth occurred, with extrusion of small amount inspissated feces. Anterior resection performed. Large raw surface remaining after removal of mass. *Course:* One-half pack removed on 7th day; all removed on 8th day. Sinus healed in five weeks.

Discussion.—The omentum often can be employed for covering denuded intra-abdominal surfaces. When its use is feasible no problem exists. In many instances, however, the omentum is short or rudimentary. Even when the omentum is well developed, it is sometimes difficult to use it satisfactorily in covering a large area, especially in the upper colonic gutters. In addition, there is some risk of subsequent obstruction when the omentum is sutured to a fixed point.

The modified Mikulicz pack accomplishes several things simultaneously: First, it serves as a framework for the immediate formation of a protective wall of granulating tissue. It has the effect of limiting the spread of infection from a given area by establishing a counter-reaction in which the surrounding viscera adhere and seal off the general peritoneal cavity. Second, it prevents the contact of the small intestines with an unperitonealized surface during the period in which the peritoneum is reacting to the trauma of mobilization and combatting the infection. Third, the pack acts as a drain. During the first few postoperative days, large quantities of serosanguineous fluid saturate the dressings. This fluid escapes about the imbrications of the rubber dam and acts as a continuous irrigation. The central gauze packing acts only as bulk and has little to do with drainage.

When the pack is removed entirely on the eighth to the eleventh postoperative day, a clean, pliable, granulating surface remains. There is practically no retention of purulent fluid at the bottom of the cavity.

When faced with an adherent inflammatory mass, the surgeon frequently

has to decide whether to proceed with an extensive mobilization, or to be content with a palliative procedure. The risks of the first alternative are greatly lessened by the use of the Mikulicz pack, and more patients may be given a chance for cure. We are certain that the pack has saved the lives of many patients who would have died of peritonitis and obstruction without it.

We have not noticed any of the disadvantages of the pack mentioned in the literature. No herniae of the abdominal wound have been observed at the point of exit of the pack. This we attribute to the use of alloy steel wire in wound closure. No enterocutaneous fistulae have occurred attributable to its use. There have been no residual abscesses or persistent sinuses. These must be guarded against by daily postoperative attention to the wound until the sinuses are completely filled in.

REFERENCES

- ¹ von Mikulicz, J.: Über die Anschaltung todter Raume ans der Peritonealhöle, *etc.*, Arch. f. klin. chir., **34**, 635-657, 1886.
- ² Faure, J. L.: Mikulicz Drain. La medecine, **5**, 524-526, April, 1924.
- ³ Madrid, A.: Faure's Technic for Mikulicz Drain. Presse med., **33**, 1289-1290, September 26, 1925.
- ⁴ Faure, J. L.: La Mikulicz. Rinasc. med., **7**, 59-60, February 1, 1930.
- ⁵ Decio, C.: A proposito del drenaggio abdominale alla Mikulicz. Rassegna d'ostet. e ginec., **37**, 69-78, 1928.
- ⁶ Cosma, R.: Il drenaggio alla Mikulicz nella chirurgia abdominale ginecologica. Ann. d'ostet. e ginec., **53**, 2039-2116, December 31, 1931.
- ⁷ Patti, P.: Sul drenaggio alla Mikulicz. Rassegna d'ostet. e ginec., **40**, 166-176, March 31, 1931.
- ⁸ Salvini, Antonio: Note cliniche sull'uso del drenaggio alla Mikulicz nella chirurgia abdominale ginecologica. Ginecologia, **2**, 285-304, April, 1936.
- ⁹ Dogliotti, Vincenzo: Considerazioni sull'uso del drenaggio alla Mikulicz nella chirurgia abdominale ginecologica. Rivista Italiana di ginecologica, **14**, 290-306, 1933.
- ¹⁰ Huguier, Alphonse: Les indications du drainage à la Mikulicz dans les interventions pelviennes. Paris Chir., **17**, 118-128, 1925.
- ¹¹ Rouhier, G.: Indications for Mikulicz Drain. Medicine, **6**, 44-49, October, 1924.
- ¹² Andre, H. C. G.: Le drainage de l'abdomen par la méthode de Mikulicz. Paris Theses, 1926.
- ¹³ Villard, E.: Mode d'action et indications du tamponnement de Mikulicz. Gazette des Hospitoux, **100**, 929-932, July 13, 1927.
- ¹⁴ Audain, Georges: Utilite et indications du drainage par meches: Que penser du Mikulicz? Progres med., **42**, 621-622, April 23, 1927.
- ¹⁵ Chaton, M.: Relections sur le Mikulicz et les drainages par meche. Bull. et mem. Soc. nat. de chir., **53**, 296-300, March 12, 1927.
- ¹⁶ Sabadini, L.: Traitement des pyosalpinx rompus en peritoine libre avec peritonite generalisse par la method conservatrice. Presse med., **40**, 1334-1336, August, 1932.
- ¹⁷ Sabadini, L.: Des ruptures de pyosalpinx en peritoine libre, et specialement de leur traitement par laparotomy simple et application d'un Mikulicz. Revué de chir., **66**, 629-646, 1928.
- ¹⁸ Dambrin, C., and Thomas: Fibrome volumineux inclus dans le ligament large; hysterectomie sur le drainage a la Mikulicz. Bull. Soc. d'obst. et de gynéc. de Paris, **18**, 649, 1929.

- ¹⁹ Lecerle, M.: A propos de Mikulicz. Bull. et mem. Soc. nat. de chir., 56, 193-195, 1928.
- ²⁰ Lazarides, M.: Sur 4 cases d'interventions abdominales septiques avec application de Mikulicz. Bull. et mem. Soc. nat. de chir., 54, 189-195, February 18, 1928.
- ²¹ Perrin, M.: Fistules, sigmoïdo-vesicale et vesico-cutanee a la suite d'un drainage abdominal a la Mikulicz. Lyon chir., 32, 581-583, 1935.
- ²² Keller, R.: Drainage et thrombose. Bull. Soc. d'obstet. et de gynéc. de Paris, 26, 253-255, 1937.
- ²³ Massabrau, G.: Une complication peu connue due drainage pelvien par la methode de Mikulicz; les abces residuels. Montpellier med., 13, 3-11, January, 1938.
- ²⁴ Lascaux, R.: La fausse conception du drainage et les bien faits du Mikulicz en chirurgie abdominale. Presse med., 40, 1219-1293, 1932.
- ²⁵ Rousseaux, R.: Pyosalpinx, perfore en peritoine libre; hysterectomie subtotale; Mikulicz guerison. Bull. Soc. d'obst. et de gynéc. de Paris, 21, 571-574. October, 1932.
- ²⁶ Alcorto, Richard: A proposito del Mikulicz en las operaciones de cancer uterine. Clin. y Laboratorio, 21, 315-317, 1932.
- ²⁷ Grigoriu, C. R., and Popoviciu, T.: Disadvantages of Mikulicz Drainage in Gynecological Operations. Endocrinol. ginec. obst., 3, 14-17, May, 1938.
- ²⁸ Andrieu, H.: Les indications du drainage au Mikulicz. Arch de med. et pharm. mil., 100, 55-78, January, 1934.
- ²⁹ Pauchet, V.: Le Mikulicz method. J. de med. de Paris, 47, 795-799, October 4, 1928.
- ³⁰ Berger, J.: A propos du Mikulicz. Bull. et mem. de la Soc. nat. de chir., 53, 213-221, February 26, 1927.
- ³¹ Cadenet, F. M.: Le drainage par le Mikulicz. Bull. mem. Soc. nat. de chir., 52, 1245-1248, 1926.
- ³² Corachan, M., and Armangue, M.: El drenaje Mikulicz en la gastrectomia. Estudio clinico y bacteriologico. Congres International de chirurgie, 2, 204-297, July, 1929.
- ³³ Gibson, C. L.: The Rubber Dam Mikulicz Tampon. ANNALS OF SURGERY, 73, 470-472, April, 1921.
- ³⁴ Farr, C. E.: The Gibson-Mikulicz Tampon in Acute Appendicitis. ANNALS OF SURGERY, 73, 473-476, April, 1921.
- ³⁵ Weeden, W. M.: The Gibson-Mikulicz Drain in Acute Appendicitis. ANNALS OF SURGERY, 88, 76-79, July, 1928.
- ³⁶ Kennedy, J. W.: Practical Surgery of the Abdominal and Pelvic Organs. Philadelphia: F. A. Davis Co., 1937.
- ³⁷ Coffey, R. C.: Application of the Principle of the Quarantine in Abdominal Surgery. ANNALS OF SURGERY, 85, 808-821, 1927.

REDUCTION OF THE MORTALITY IN THE SURGICAL MANAGEMENT OF HYPERTHYROIDISM: THE USE OF THE SHORT INTERVAL TWO-STAGE LOBECTOMY

W. C. SEALY, M.D., AND H. B. KERNODLE, M.D.

DURHAM, N. C.

FROM THE DEPARTMENT OF SURGERY, DUKE UNIVERSITY SCHOOL OF MEDICINE, DURHAM, N. C.

THE MORTALITY in the surgical management of hyperthyroidism has been lowered to the level of a very safe surgical procedure since the use of iodine in the preoperative management of this disease. This serves primarily to reduce temporarily the degree of hyperthyroidism, so that the postoperative reactions are of a much milder degree. In this manner the principal cause of death in these cases is controlled. Still, there is a small group of severely toxic patients, in spite of the relative decrease in the basal metabolic rate, that have alarming postoperative reactions. It is in this group of cases that most of the deaths occur. As a result of these severe toxic reactions, patients succumb from the effect on the visceral structures. A well compensated heart or liver may be damaged to such an extent by a severe reaction that death results; or moderate reactions may be enough to cause a fatality when associated with an already damaged heart or liver. This was demonstrated in this clinic by a recently reported study on the effect of infection on the liver of hyperthyroid animals.¹

In 1938, the Surgical Staff at Duke Hospital reviewed the results for the thyroidectomies for hyperthyroidism. The total mortality was found to be 6.94 per cent, and still more significant was the 15.6 per cent mortality in the nodular toxic group. In order to reduce this high figure, a more careful plan of preoperative management was instituted; and a selected group of cases were operated upon in multiple stages. It was not found necessary to do any pole ligations, and all were undertaken as lobectomies. From this change in the management of these cases the mortality was markedly reduced.

No radical change was made in the preoperative preparation other than more careful attention to the details in the management. The patients were placed in a private room at complete bed rest. Iodine and sedation along with a high vitamin, high caloric, high protein, and high carbohydrate dietary regimen was employed. Careful attention was paid to the cardiac and liver status and measures were instituted to prevent complications from poor function of these structures. In choosing the time for operation, the general condition of the patient, the pulse rate, and basal metabolic rate were all considered; and as long as the patient showed improvement, operation was delayed. Some of the patients were prepared for as long as 21 days.

Before 1938 an occasional case had been operated upon in multiple stages (2.43 per cent), with an interval of six weeks between stages. Because of the economic conditions of most of our patients, it was found that this method was not satisfactory. On admission for the second operation the basal

metabolic rate was found to be about the same level as on the previous admission. The patients were difficult to follow and to get back to the hospital, because of the long distances they lived from the hospital. After reading the paper of McGraw,² in 1938, it was decided to use the short interval two-stage procedure with 10 to 12 days between each stage.

McGraw reported 161 cases operated upon in multiple stages, with 10 to 12 days between stages that included not only lobectomies but pole ligations. In this group there was a mortality of 7.5 per cent; but in the group that had lobectomies, there was only one death in 48 cases. The incidence of infection was very high (17 per cent for the 161 cases). McGraw did not report any marked reduction in the basal metabolic rate following the first stage. In 1939, Taffel and Harvey³ reported 52 cases operated upon at intervals of 5 to 15 days, with one death following the first stage. There were three infections in the group, one stitch abscess, one severe infection, and one infected hematoma. Following the first stage there was an average drop in the basal metabolic rate of 14. Both of these clinics used the same incision for the second operation.

By the use of careful preoperative management of hyperthyroid patients, we did not find it necessary to do any pole ligations but were able to perform a lobectomy at each stage. After using the method for a time many advantages were apparent, in addition to the ones already listed. We found that there was a lowering of the basal metabolic rate between stages, and, technically, the operation was much easier at this time than at an interval of six weeks. With the use of ultraviolet radiation⁴ there were no infections in the group operated upon in two stages.

It is difficult to describe the indications for a two-stage operation as so much depends on clinical observation and judgment. The evaluation of the patient on entering the clinic is the one factor that bears most weight, as has been stressed by Lahey.⁵ A second factor is the patient's response to iodine, rest, and sedation; as measured by the basal metabolic rate, pulse rate, weight, and nervousness. A third factor is the status of the liver, cardiovascular system, and other organs. Other factors are the age, admission basal metabolic rate, duration of the disease, and mental changes. The decision in favor of a two-stage operation was made occasionally at the time of operation because of (1) a tachycardia under anesthesia as high as 180 to 200; (2) a high pulse pressure; and (3) a large consumption of oxygen. In summary, the two-stage operation was elected whenever the preoperative studies or the reaction of the patient to the operative procedure indicated the probability of a severe postoperative reaction.

The operative technic was the same as has always been employed in the one-stage procedure. Silk was used throughout, using both subcutaneous and cutaneous sutures. The incision was reopened for the second stage and again closed with silk. No drains were inserted at either operation.

The change in handling the cases of hyperthyroidism at Duke Hospital

HYPERTHYROIDISM

took place about January 1, 1939. The results of all operations for hyperthyroidism performed before this time are compared with the ones after this date. Table I shows the comparison of the mortality along with the per cent of two-stage procedures during these two periods. In the 201 cases operated upon before 1939, the mortality was 6.94 per cent while only 2.43 per cent of the cases were operated upon in multiple stages, with a mortality of 1.7 per cent. In the nodular toxic group the reduction of the mortality was still more marked, changing from 15.6 per cent, before 1939, to 2.77 per cent after this date (Table II). It was in this group of cases that the main reduction in the mortality took place.

TABLE I
THE MORTALITY AND PER CENT OF TWO-STAGE OPERATIONS
Performed Before and After January 1, 1939

Time	No. of Cases	Deaths	Mortality Per Cent	Percentage of Total Operations Performed in Two Stages
Before 1/1/39.....	201	14	6.94%	2.43%
After 1/1/39.....	176	3	1.7%	14.7%

TABLE II
THE POSTOPERATIVE MORTALITY IN TOXIC NODULAR AND TOXIC DIFFUSE GOITERS
Before and After January 1, 1939

Type of Goiter	No. of Cases	Deaths	Mortality Per Cent
Nodular toxic before 1/1/39.....	64	12	15.6%
Nodular toxic after 1/1/39.....	72	2	2.77%
Diffuse toxic before 1/1/39.....	137	2	1.46%
Diffuse toxic after 1/1/39.....	104	1	0.95%

In summarizing all the causes of death, it is seen that the thyroid crisis, or storm, is the principal reason, resulting in 63.5 per cent, or in 11 of the 17 deaths. The other causes of death are incident to any major surgical procedure. After January 1, 1939, there was only one case dying as a result of a postoperative thyroid crisis and this case was operated upon as a one-stage procedure. The causes of death are listed in Table III.

TABLE III
THE CAUSE OF DEATH FOLLOWING OPERATION FOR ALL CASES
Before and After 1939

Cause of Death	No. of Deaths	Mortality Per Cent
Postoperative thyroid crisis.....	11*	63.53%
Died on operating table.....	2*	11.77%
Cerebral embolus.....	1	5.82%
Pulmonary embolus.....	1	5.82%
Bronchiopneumonia.....	1	5.82%
Coronary occlusion.....	1*	5.82%
Total of three cases.		5.82%

Of the 25 cases operated upon in multiple stages there was only one death. This occurred during the first operation from what was thought to be ventricular fibrillation from cyclopropane anesthesia, as the patient was fibrillating before operation. As a result of this we began to employ ether in all cases having cardiac complications. The one death in this

group gave a mortality of four per cent, but the mortality in this group is bound to be high as this is a select group of poor risk patients. The best interpretation of the results is the effect on the overall mortality of performing two-stage operations.

Table IV shows the comparison of the basal metabolic rate of patients operated upon in one and two stages. The average basal rate was found to be plus 36.64 per cent in the cases operated upon in one stage as compared to plus 61.83 per cent average basal metabolic rate for the cases operated upon in multiple stages. Before operation the basal metabolic rate in the one-stage group fell to plus 18.52 per cent, as compared with plus 29.92 per cent in the two-stage group. The age in the two-stage group averaged two years greater than the one-stage group. The two-stage cases had cardiac damage in 43.3 per cent, and liver damage in 6.5 per cent.

TABLE IV
COMPARISON OF THE AGE OF THE PATIENT AND THE B. M. R. FOR SINGLE AND MULTIPLE-STAGE OPERATIONS
Performed After January 1, 1930

Operation	Average B. M. R. on Admission	Average B. M. R.		Average Age in Years
		Just Before Operation		
One stage	Plus 36.64%	Plus 18.52%		35.28
Two stages	Plus 61.83%	Plus 29.92%		37.2

In all our cases there was a fall in the basal metabolic rate following the first stage to a level usually lower than the last pre-operative basal rate. The average for the group was plus 24.1 per cent when recorded on the 8th to 10 postoperative day. All the patients were kept on iodine following the first stage operation.

CONCLUSIONS

Deaths following thyroidectomies for hyperthyroidism, in the majority of cases, are due to postoperative thyroid reactions. The incidence of severe reactions has been reduced by the employment of iodine in the preparation of these patients for operation. In a small group of seriously ill patients the operative mortality is still quite high as a result of thyroid crises. If the mortality for the entire group is to be reduced, then measures directed toward the prevention of these reactions is necessary. Our experience, since 1939, has shown that careful and detailed preoperative care followed by use of two-stage operations in the more seriously ill patients will reduce the incidence and severity of thyroid crises. When this reduction in the postoperative reactions takes place, then the mortality falls. As one performs more operations in two stages there is a reduction in the mortality. The significant fact in the mortality figures is not the deaths in the two-stage operations, but the reduction in the mortality of all cases of hyperthyroidism operated upon.

A two-stage operation should be undertaken in all poor risk patients. As Lahey⁵ has stated, any patient that has a severe postoperative reaction should have been operated upon in two stages. At Duke Hospital we have

HYPERTHYROIDISM

not performed any pole ligations nor have we undertaken any operations upon thyroid patients as emergency procedures. If a patient cannot be brought into condition to stand a lobectomy, operation had better be deferred, as by careful handling nearly all can be improved to such an extent that surgery can be undertaken. The ones that do not improve stand no chance of surviving a surgical procedure.

The two-stage lobectomy performed at 10 to 12 days between stages, has proved to be the most satisfactory method of undertaking multiple-stage operations. With the employment of ultraviolet radiation there is very little danger of infection from opening the wound for the second stage. It has been our experience that the patient's basal metabolic rate is much lower at ten days than it is at the end of six weeks. The operative procedure is much easier at this time than at a later date.

SUMMARY

1. The majority of deaths following thyroidectomy for hyperthyroidism are due to thyroid crisis.
2. Measures directed toward prevention of these reactions will lower the postoperative mortality.
3. Careful preoperative management and the employment of the two-stage procedure in poor risk patients reduced the mortality at Duke Hospital from 6.94 to 1.7 per cent.
4. The short interval two-stage procedure is suggested as the best method for carrying out the two-stage operation.

REFERENCES

- ¹ Sealy, W. C.: The Induction of Liver Necrosis in Rabbits by the Combination of Experimental Hyperthyroidism and Shope Papilloma. *ANNALS OF SURGERY*, 113, 572-578, April, 1941.
- ² McGraw, A. B.: Short Interval Stage Operations for Severe Hyperthyroidism. *ANNALS OF SURGERY*, 107, 198-206, February, 1938.
- ³ Taffel, M., and Harvey, S. C.: Short Interval Two-Stage Thyroid Lobectomy for Hyperthyroidism. *ANNALS OF SURGERY*, 109, 437-441, March, 1939.
- ⁴ Hart, Deryl, and Upchurch, Samuel E.: "Unexplained" Infections in Clean Operative Wounds. *ANNALS OF SURGERY*, 114, 936-959, November, 1941.
- ⁵ Lahey, F. H.: Stage-Operations in Severe Hyperthyroidism. *ANNALS OF SURGERY*, 104, 1611-1626, December, 1936.

ECHINOCOCCUS CYST OF LUNG EXHIBITING UNUSUAL RADIOLOGIC AND SURGICAL FEATURES

CLIFFORD D. BENSON, M.D., WILLIAM A. EVANS, JR., M.D.,

AND

WOLF W. ZUELZER, M.D.

DETROIT, MICH.

FROM THE CHILDREN'S HOSPITAL OF MICHIGAN AND WAYNE UNIVERSITY, COLLEGE OF MEDICINE, DETROIT, MICH.

ALTHOUGH echinococcus disease is rare in this country, it is common in Australia, Iceland and the Argentine. Next to the liver, the lung is the most frequent site of localization of hydatid cysts. Their location in the lung may be central or peripheric, and the latter type may increase in size to such an extent that contact with pleura occurs. With the extension to the pleura, pleural pain is of frequent occurrence and may be the only symptom causing the patient to seek medical aid.

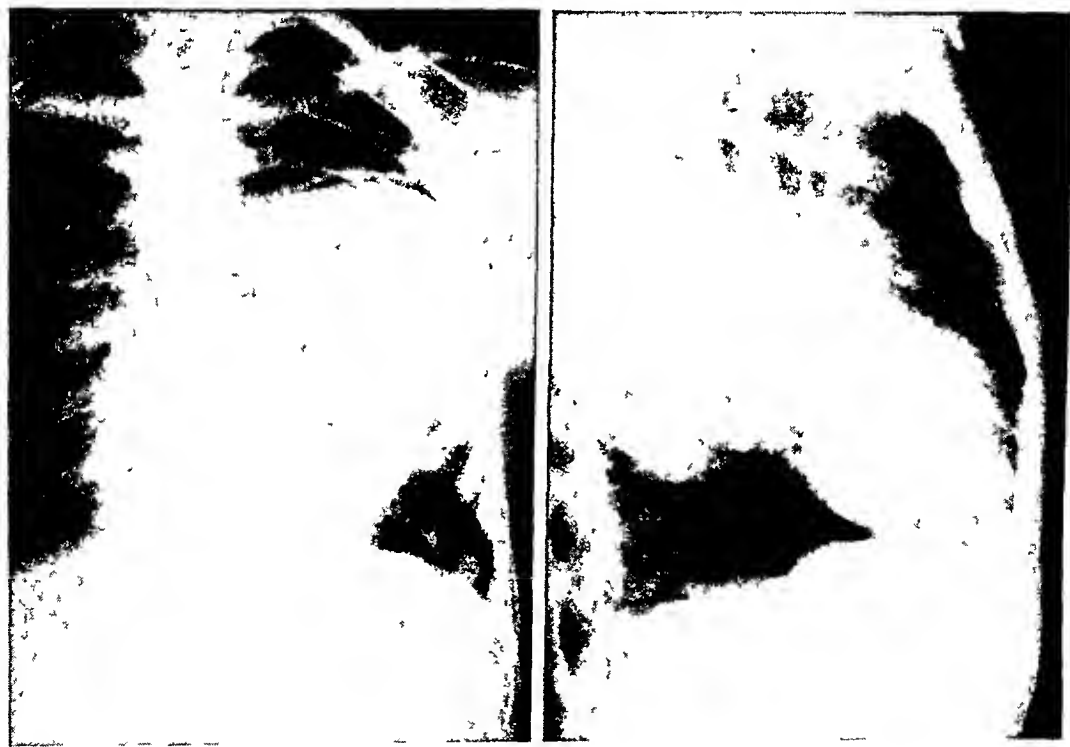


FIG 1.—Radiograms exposed in postero anterior and right lateral projections showing the large ovoid mass of the hydatid vesicle separated from the capsule of the adventitia by a crescentic air space superiorly and to a lesser extent inferiorly.

The case we are reporting is of particular interest as it illustrates a radiologic manifestation which has been regarded by South American writers as a pathognomonic sign, and because of the unique surgical experience in treating the patient.

Case Report.—R. DeL., white, male, age 12, had lived in Italy until coming to the United States in 1937. He was admitted to the Children's Hospital of Michigan, March 16, 1942, complaining of a pain in the left side of the chest in the region of the

ECHINOCOCCUS OF LUNG

midaxillary line, accompanied by a dry cough of ten days' duration. There had been some progressive loss in weight, weakness and pallor for about six months. He was said to have had a similar attack of pain and cough with some fever in the preceding year.

The physical examination disclosed dullness on percussion of the left side of the chest posteriorly, with diminished breath sounds and fine râles at the base. The temperature, pulse and respirations were normal, as were the routine laboratory studies of the blood and urine. There was no eosinophilia. The tuberculin skin test and the Kline test for syphilis were negative.

Radiologic examination, March 16, 1942, disclosed a sharply circumscribed shadow in the left midchest posteriorly, measuring 10.5 x 8.5 cm. (Fig. 1). The shadow was of uniform density except for the appearance of a capsule at the periphery, with a layer of air between the capsule and the mass itself. This phenomenon was not explained, and a presumptive diagnosis of a benign tumor was made. Upon reexamina-



FIG. 2.—Reexamination following the creation of an artificial pneumothorax on the left. The air space beneath the capsule has disappeared.

tion one week later, following the production of a diagnostic pneumothorax, the air beneath the capsule was no longer seen (Fig. 2). The mass appeared to be separated from the parietal pleura at the lateral chest wall. At a third study, immediately preceding the operation, the pneumothorax had disappeared and there was again no sign of a capsule or any other differentiating shadow within the mass.

Operation.—April 4, 1942: Dr. Clifford D. Benson and Dr. Grover C. Penberthy. The left pleural cavity was entered through a posterior approach after resecting a portion of the fifth and sixth ribs. The lower lobe, containing the mass, was adherent posterolaterally to the parietal pleura (Fig. 3). These adhesions were easily separated. On exploration, a cyst was found at the periphery of the lung completely surrounded by pulmonary tissue except in an area 4 x 3 cm. on the lateral side. At this point it seemed covered only by a thick membrane which was incised for 4 cm. The edges of the cut membrane were retracted and a thin, white-walled cyst was exposed (Fig. 4).

Film-like adhesions between the cyst and outer membrane were separated carefully, allowing the complete removal of the pulmonary cyst intact (Fig. 5).

After the cyst was enucleated, a small bronchial fistula was seen in the depth of the adventitial pouch (Fig. 6). The outer membrane was excised and the fistula and defect in the lower lobe were obliterated by suturing the pulmonary tissue in three layers with interrupted chromic catgut. A Pezzar catheter was inserted in the eighth interspace and connected to a tube under water to allow for any drainage of



FIG. 3.—A. Demonstrates the surgical approach and relative position of the cystic mass. B. Operative sketch showing the left pleural cavity and cyst. Note the adhesions between the outer membrane and parietal pleura.

fluid or air. During the operative procedure the patient received 300 cc. of blood and 250 cc. of 5 per cent dextrose solution intravenously. The operative wound in the chest wall was closed in layers and healed *per primam*. The postoperative course was uneventful, with gradual complete reexpansion of the lung. The catheter was removed from the pleural cavity, May 6, 1942, and the patient discharged from the hospital in good condition May 8, 1942.

ECHINOCOCCUS OF LUNG

Pathologic Examination.—The material submitted for pathologic examination consisted of two specimens. One was a large thin-walled cyst of oval shape, measuring 10 x 8 x 8 cm. (Fig. 5). The outer cyst wall was fairly smooth except for a few thin tags and strands. The cyst wall was translucent and of jelly-like consistency. Within a few minutes after removal the cyst ruptured spontaneously, discharging approximately 200 cc. of a clear fluid containing a heavy, turbid, whitish sediment which settled rapidly. The inner surface of the cyst wall was finely granular. The fluid had a spe-

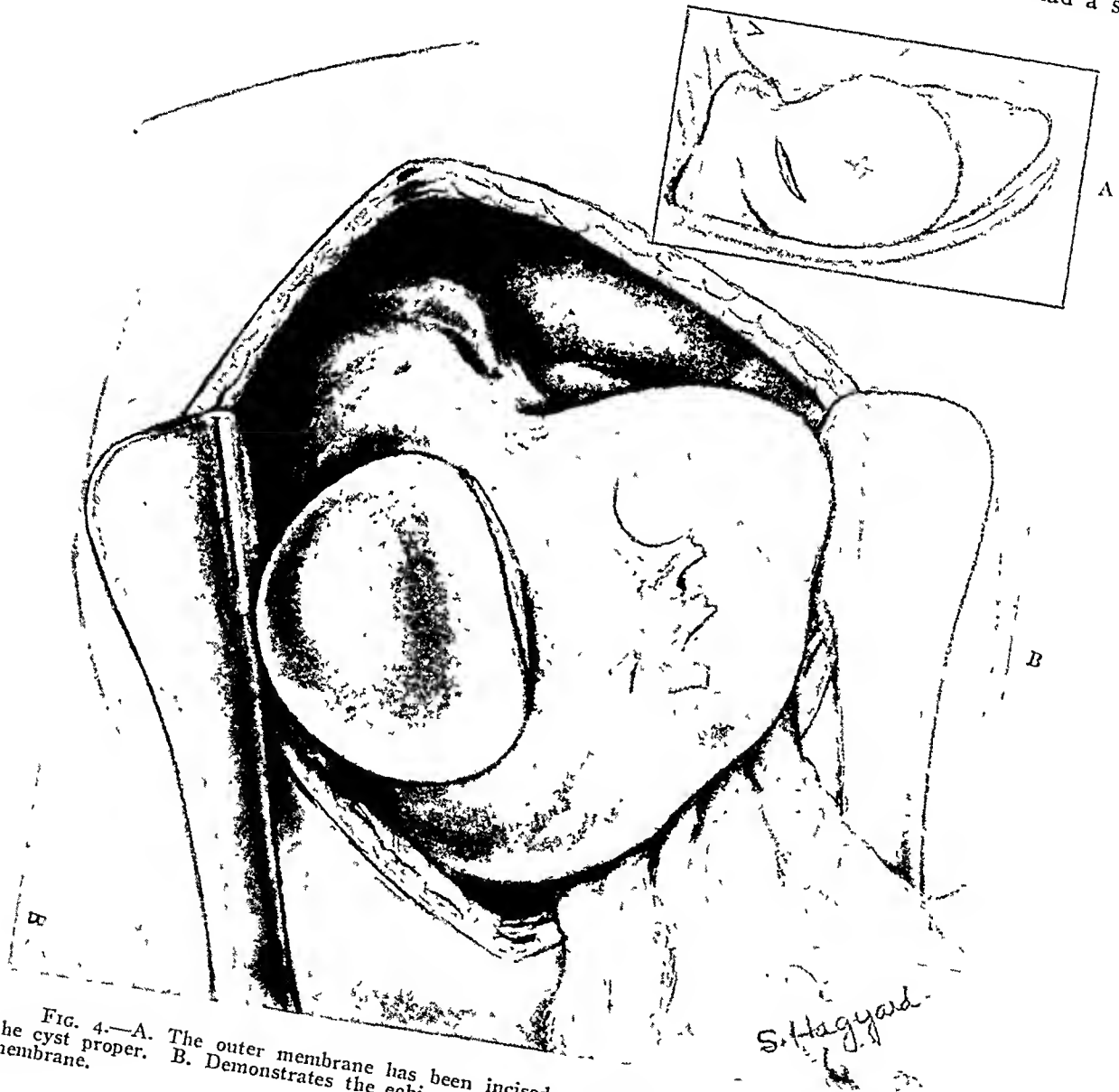


FIG. 4.—A. The outer membrane has been incised exposing the thin white membrane of the cyst proper. B. Demonstrates the echinococcus cyst being removed from within the outer membrane.

cific gravity of 1.012, and a weakly alkaline reaction. It contained no sugar and only a faint trace of albumin (probably due to contamination with blood from a piece of rib contained in the same jar). The sediment was loaded with well preserved scolices having the characteristic appearance of *Taenia echinococcus* (Fig. 7). The rostellum was usually inverted, occasionally everted, with distinct suction cups. In a few instances there was beginning segmentation. Here and there free hooklets were found. Microscopic examination revealed a thin, wrinkled, structureless membrane, with a loose cellular

inner layer lined with a sort of basement membrane. On thin projections of this membrane the scolices were attached, like wine glasses on their stems.

The second specimen consisted of a tough, firm, grayish-pink membrane, measuring 11 x 7 cm., varying in thickness from 0.1 to 0.4 cm. Both surfaces were rough and shaggy, and soft hemorrhagic thickenings were present on one side.

On microscopic examination the surface of this outer membrane facing the cyst was composed of dense acellular fibers of collagen. Farther outward this membrane became slightly cellular and was loosely infiltrated with plasma cells, lymphocytes and occasional eosinophilic leukocytes. There were a few capillaries in this region and occasional cleft-like compressed spaces lined with cuboidal or columnar epithelium resembling the lining of bronchioles. In a few areas the fibrous tissue of the membrane divided into two layers enclosing compressed, atelectatic alveoli. In several sections



FIG 5—Photograph of the intact cyst after removal

the membrane had no outer limiting layer. In one section, however, lung tissue was attached to the outer surface of the fibrous membrane. The lumen of the alveoli was for the most part considerably reduced and there was fresh hemorrhage into many air sacs, probably incidental to the operative procedure. The pleural surface of the lung was included on the side opposite the fibrous membrane. The pleura was thickened by fibrous tissue and in some areas there was considerable hemorrhage and exudation of fibrin on the mesothelial surface. Underneath the surface the mesothelial cells had proliferated.

DISCUSSION

Pathologic Aspects.—The cyst was a typical hydatid echinococcus. The thin-walled cystic mass first removed was the parasite itself. The delicate friable walls represented the so-called brood membrane of the parasite proper

to which numerous living scolices were attached. The fluid had the characteristics of echinococcus fluid and contained large numbers of free living scolices. The tough outer membrane, the adventitia, was formed by compressed, condensed and collagenized lung tissue with an inflammatory reaction. The surrounding alveoli were atelectatic and there was an acute and chronic pleurisy in the overlying pleura. All these features were entirely characteristic of a hydatid *Taenia echinococcus* developing in the lung.

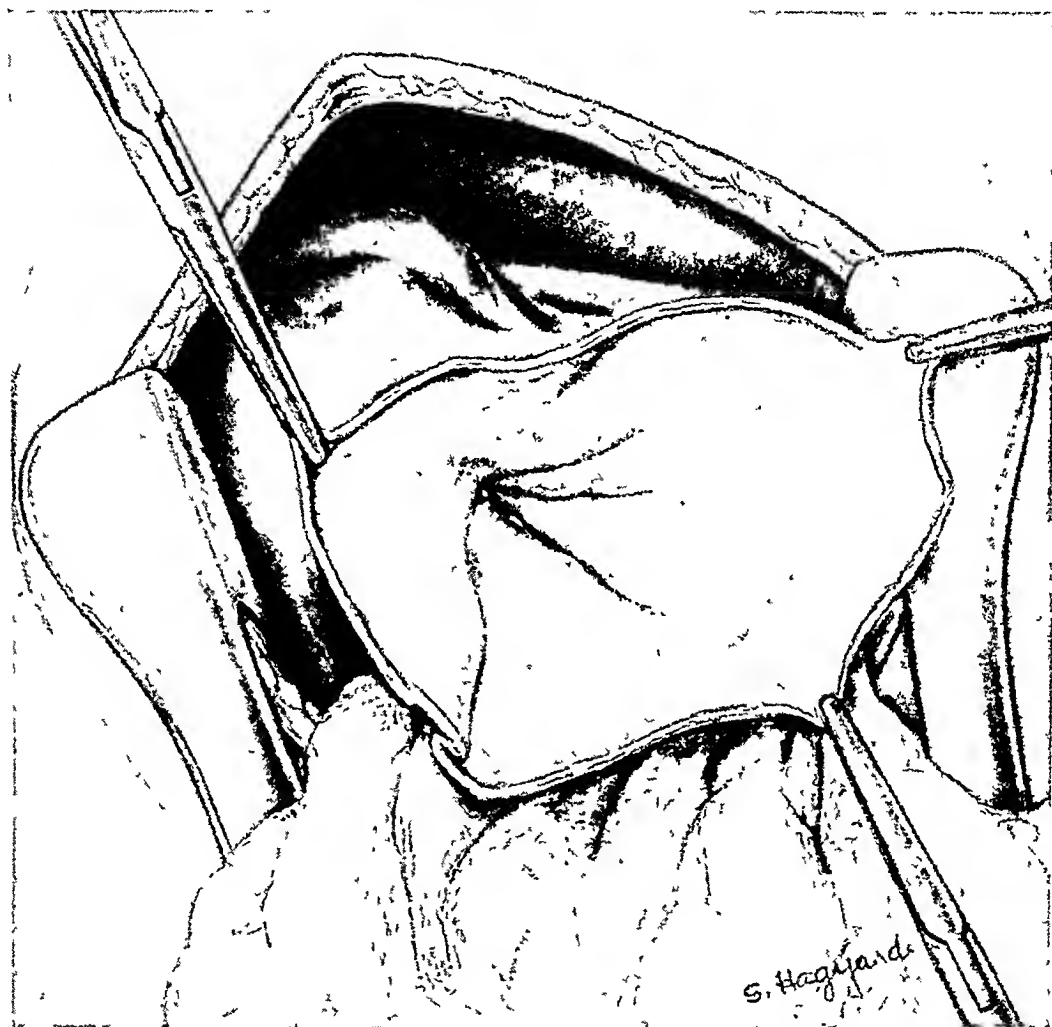


FIG. 6.—Drawing of the outer membrane remaining after removal of the cyst showing the small bronchial fistula.

Surgical Aspects.—An excellent review of the history and development of the surgical treatment of pulmonary echinococcus cysts has recently been published in English by Arce.³ In the light of this material, the case we are reporting is of unusual interest in that it was possible to remove the entire intrapulmonary cyst *intact*. Furthermore, the fistulous communication between a bronchus and the pericystic space beneath the adventitia, which accounted for the crescentic air chamber observed radiographically, was clearly demonstrated. Finally, the bronchial fistula remained closed after the surgical repair of the pulmonary defect incident to removal of the cyst.

Radiologic Aspects.—Echinococcus cysts of the lung, during the course

of their development and disintegration, exhibit an interesting variety of radiographic manifestations some of which are quite pathognomonic. The description of the radiographic appearance of pulmonary echinococcus disease goes back at least as far as 1899, when Levy-Dorn and Zadek¹ reported a case and differentiated between the simple unruptured cyst and one which had been evacuated. The classic description of a simple echinococcus cyst as a rounded shadow of uniform density and sharp outline in the clear pulmonary field is usually ascribed to M. A. Bécclère (1903),² who considered

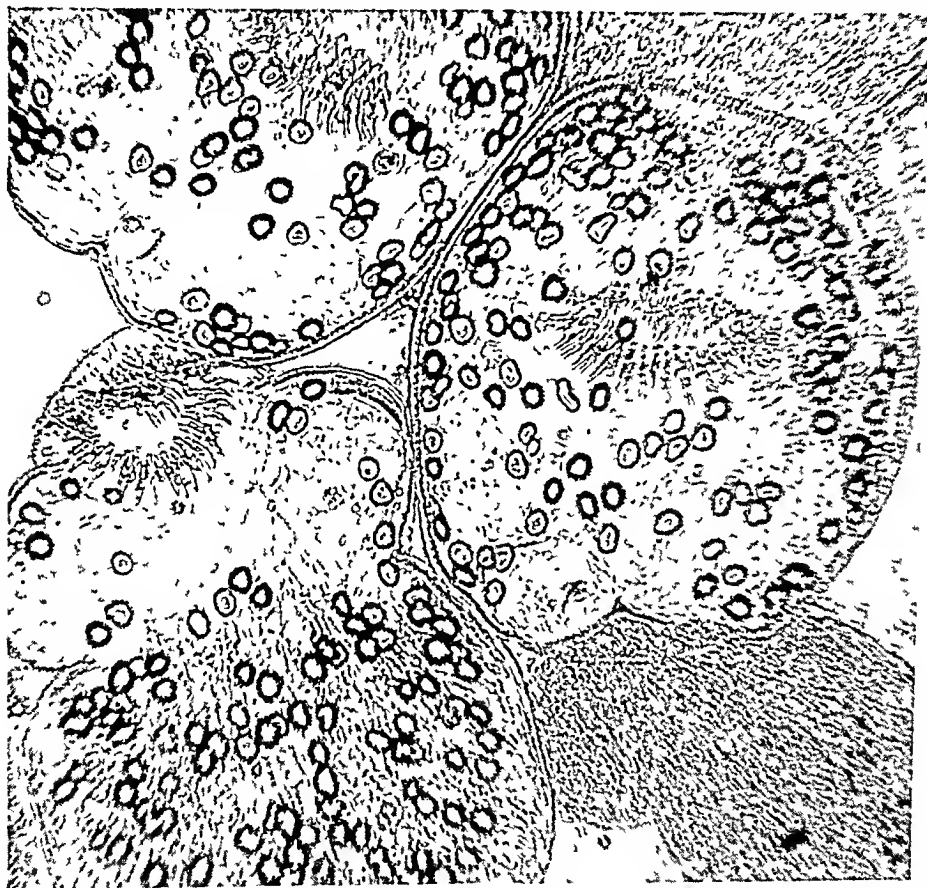


FIG 7.—Photomicrograph of scolices obtained from the cystic fluid

this picture as pathognomonic. However, in this stage of development of the cyst a positive radiologic diagnosis cannot be made, for differentiation may be impossible from neoplasms such as sarcomata, either primary or secondary, and occasionally chondromata and osteomata as well as carcinomata, neurinomata and fibromata. Rarely, certain inflammatory granulomata, such as the gumma of syphilis, dermoids and other congenital cysts, lymphogranulomata and even aneurysms may produce a similar appearance.

As the echinococcus cyst increases in size, the circular contour may be deformed through the resistance offered by the chest wall, the diaphragm or the bronchi. Escudero and later Nemenov⁴ observed that hydatid cysts in contrast to solid tumors may change their shape during respiration and

this manifestation is known as the sign of Escudero-Nemenov. Large cysts tend to produce an enlargement of that portion of the thorax in which they lie with displacement of the mediastinal structures to the opposite side. This behavior is in contrast to that of tumors which are more apt to produce massive atelectasis and contraction of the chest and is referred to as the sign of Querilo-Walsch. Cysts, in contrast to aneurysms, do not produce erosion of bone. The outline of the cyst is not always sharp and particularly in older cysts there may be varying degrees of inflammation and atelectasis in the lung adjacent to the adventitia of the cyst giving an indistinct feathered outline. If the pleura is near the cyst a marked pleural reaction may develop. Although the adventitia may become very dense and sclerotic it rarely becomes calcified, in contrast to hepatic hydatids.

As the cyst enlarges bronchial communication may develop in the adventitia and upon coughing or other forceful expiration a small amount of air may enter the space between the membrane of the hydatid vesicle which is part of the parasite proper and the adventitia which is formed by the host. Like the pleural space, this space is originally present as a virtual one only. According to Dévé,⁵ the great French authority on echinococcus disease, this manifestation of air between the membranes was first observed radiographically by Zehbe,⁶ in 1916. It was subsequently described by others but its significance and diagnostic importance was not appreciated until interest was aroused by the reports of Caeriro and Goyena,⁷ of Buenos Aires, in 1933, and independently by Morquio, Bonaba, and Soto,⁸ of Montevideo, in 1934. The latter group, which had observed five cases in about two years, gave the designation perivesicular pneumocyst to the phenomenon, and recognized that it was reversible. The parasite remains intact, with no escape or alteration of the contents of the cyst fluid. Belot and Peuteuil⁹ reported the condition from Algiers, in 1936, as the "sign of detachment," and there were other reports from Nguyen-Dinh-Hoang,¹⁰ Constantini and LeGénissel,¹¹ Guarini,¹² Ivanissevich and Ferrari,¹³ Cantonnet Blanch, Charbone, and Barberousse,¹⁴ Chifflet and Purriel,¹⁵ Brun, Jaubert de Beaujeu and Bège,¹⁶ Andrade,¹⁷ Rivas and Gobich,¹⁸ and others. Ivanissevich and Ferrari¹³ were able to produce the condition experimentally by insufflating the trachea of a sheep affected with pulmonary echinococcosis. Chifflet and Purriel¹⁵ observed that the sign may be brought out only on deep inspiration. Other terms used for the phenomenon are *cámara aerea* or air chamber, *calotte aeriennne* or air cap, crescent image, periparasitic emphysema, pneumoperihydatid and pericystic emphysema. The phenomenon is generally regarded as a rare manifestation of pulmonary echinococcus but quite pathognomonic when it does occur. Constantini and LeGénissel¹¹ found it in only three of 100 cases reviewed by them. Dévé⁵ observed a similar picture in a case of aspergillosis in which a mass of fungi, a mycelial calculus, almost filled a large bronchiectatic abscess, leaving only a thin layer of air. The mass however did not have the hair-line sharpness of a hydatid vesicle, and he regarded his case as "an

exception which proved the rule" concerning the pathognomonic validity of the sign.

Although the phenomenon of pericystic air space is reversible, it usually indicates the imminent disintegration and rupture of the vesicle and the subsequent evacuation of the cystic fluid and membranes through a bronchus ("vomica"). This is well illustrated in the serial studies of cases reported by Constantini and LeGénissel.¹¹ Presumably the detachment of the cyst results in impaired nutrition leading to the death of the parasite. As the fluid escapes from the cyst a fluid level is formed in the pericystic space and the brood membrane falls away from the adventitia and is recognized in the radiogram as an arch between the adventitia and the fluid level. This stage was first described by Cumbo, in 1921, hence known as Cumbo's sign, later by Tillier,¹⁹ in 1932, Blefari-Melazzi,²⁰ in 1933, and by Ivanissevich and Ferrari¹³ who referred to the roentgen appearance as the "double arc sign." Rivas and Gobich¹⁸ observed the "double arc sign" three times in 150 cases encountered over a period of about 20 years.

When the cyst ruptures the fluid becomes infected, and the term pyopneumocyst is commonly used. As the vesicular membrane collapses further it becomes an irregular mass floating on the fluid. This produces the "sign of the *camalote*" (a South American river weed of the family of the Iridaceae, resembling a water lily) described by Segers²¹ and Lagos Garcia, in 1924. Differentiation from the common pyogenic lung abscess may be difficult at this stage. According to Tillier¹⁹ the recognition of the retained membrane and the slow movement of the fluid on change of position, which is due to the presence of the membrane rather than actual viscosity of the fluid, permit the diagnosis of echinococcus disease. A final manifestation is the expectoration of the cystic fluid and fragments of the membrane. The diagnosis can then be made upon identification of the hooklets or the membrane. The entire parasite may be evacuated in this manner and a spontaneous cure result.

SUMMARY

Successful surgical excision of an echinococcus cyst of the lung by a single-stage procedure is reported. The radiologic manifestation due to the presence of air between the parasite and the adventitia was present. A small bronchial fistula accounting for the latter phenomenon was demonstrated at operation. The recognition of this radiologic sign will lead to early diagnosis of hydatid cyst of the lung and, if followed by surgical excision of the cyst intact, will eliminate complications due to the rupture of the cyst and multiple-stage operative procedures in an attempt to cure the disease.

BIBLIOGRAPHY

- 1 Levy-Dorn and Zadek: Zur Untersuchung mit Roentgenstrahlen bei Lungenechinococcus. Berl. Klin. Wchschr., 36, 431, 1899.
- 2 Bécélère, M. A.: Un cas de kyste hydatique du poudmon gauche, avec présentation de stéréo-radiogrammes. Bull. et mém. Soc. méd. d. hôp. de Paris, 20, 763, 1903.

- ³ Arce, M., Arce, F.: Estudio radiológico de la equinococosis pulmonar. Barcelona, 1941.
- ⁴ Nemenov: Zur Roentgendiagnostik der Echinokokkus, insbesondere der Bauchhöhle. Verhandl. d. deutsch. Roentgen-gesellsch., 13, 74, 1922.
- ⁵ Dévé, F.: Le signe radiologique de la "calotte aérienne" n'est pas rigoureusement pathognomonique du kyste hydatique du poumon. An. Inst. modelo de clin. méd., 18, 7, 1937; and Semana méd., 1, 1081, 1938.
- ⁶ Zehbe, R.: Über Lungen- und Pleura-Echinokokkus. Fortschr. a. d. Geb. d. Roentgenstrahlen, 24, 63, 1916-1917.
- ⁷ Caeiro, J. A., and Goyena, J. R.: Quiste hidatídico del lóbulo superior del pulmón izquierdo. Bol. y trab. de la Soc. de cir. de Buenos Aires, 17, 144, 1933.
- ⁸ Morquio, L., Bonaba, J., and Soto, J. A.: El neumo-quiste perivesicular a mínima reparable: Nuevo signo radiológico del quiste hidatídico del pulmón. Arch. de pediat. d. Uruguay, 5, 353, 1934.
- ⁹ Belot, J., and Peuteuil, G.: Le signe du "décollement" pathognomonique du kyste hydatique du poumon. Bull. et mem. Soc. de radiol. méd. de France, 24, 533, 1936.
- ¹⁰ Nguyen-Dinh-Hoang: A propos du signe du décollement pathognomonique du kyste hydatique du poumon. Presse méd., 44, 2117, 1936.
- ¹¹ Constantini and LeGénissel: A propos de l' "image de décollement" du kyste hydatique du poumon. Bull. et mem. Soc. de radiol. med. de France, 25, 727, 1937.
- ¹² Guarini, C.: Diagnos radiológica delle cisti idatide del polmone. Arch. di radiol., 13, 460, 1937.
- ¹³ Ivanissevich, O., and Ferrari, R.: Diagnóstico radiológico de los quistes hidaticos del pulmón. Semana méd., 44, 825, 1937.
- ¹⁴ Cantonnet Blanch, P., Charlone, R., and Barberousse, C. M.: Valor diagnóstico del neumoquiste perivesicular. Arch. de pediat. d. Uruguay, 8, 387, 1937.
- ¹⁵ Chifflet, A., and Purriel, P.: El neumoquiste perivesicular. Arch. urug. de med. cir. y especialid., 11, 639, 1937.
- ¹⁶ Brun, Jaubert de Beaujeu, and Bège: Evolution rapide d'un kyste pulmonaire avec formation d' images de décollement. J. de radiol. et d'électrol., 22, 495, 1938.
- ¹⁷ Andrade, R. I. J.: Diagnóstico clínico y radiológico del quiste hidatídico del pulmón. Am. Inst. modelo de clin. med., 19, 301, 1938.
- ¹⁸ Rivas, C. I., and Gobich, E.: Equinococosis hidatidico del pulmón: El signo del doble arco de Ivanissevich. Rev. Asoc. méd. argent., 55, 689, 1941.
- ¹⁹ Tillier, R.: Le diagnostic radiologique des kystes hydatiques suppurés du poumon. Bull. et mém. Soc. de radiol. méd. de France, 20, 361, 1932.
- ²⁰ Blefari-Melazzi, T.: Contributo alla diagnosi radiologica delle immagini atipiche de cisti idatide del polmone. Arch. di radiol., 9, 257, 1933.
- ²¹ Segers, A.: Consideraciones sobre el "signo del camalote" en los pñeumo-quistes hidatídicos. Acción méd., 3, 325, 1932.
- ²² Arce, José: Hydatid Disease (Hydatidosis). Arch. Surg., 43, 789, 1941.

EVOLUTION OF SPINAL FUSION

M. B. HOWORTH, M.D.

NEW YORK, N. Y.

FROM THE NEW YORK ORTHOPAEDIC DISPENSARY AND HOSPITAL, NEW YORK, N. Y.

DISCUSSION OF THE EVOLUTION of spinal fusion must necessarily begin with the names of Russell Hibbs and Fred Albee, as these two men were the first to develop methods of spinal arthrodesis and to further the general use of these procedures by the orthopedic surgeon. Hibbs, in 1910, devised a method of using fragments from the spinous processes and laminae as a means of obtaining bony ankylosis, whereas Albee used a graft of free bone from the tibia of the patient. Hibbs had observed, in studying the pathology of tuberculosis of the spine after treatment with plaster encasements or braces, that in many cases a spontaneous bony ankylosis of the lateral articulations and occasionally of the laminae and spinous processes had occurred. Sometimes even the vertebral bodies were found to be fused together. He observed, also, that this natural ankylosis was usually incomplete, sometimes including the joint on only one side, and usually lagging behind the tuberculosis as it advanced up and down the spinal column. He found that it took many years for the ankylosis to occur, and that it rarely resulted in complete healing of the disease. Hibbs reasoned that if the ankylosis could be produced operatively, safely, and more quickly than would occur by the natural process, that the complete splinting effect afforded thereby might result in more rapid and more certain healing of the disease. He stated: "One of the reasons why the disease is so persistent in its destructive effect on the bodies of the vertebrae is because of the motion which takes place between them, and while the various methods of treatment limit the motion, none absolutely prevents it. In the light of our present knowledge and experience the greatest need in the treatment of this disease, both from the standpoint of shortening its duration and preventing its deformity, is the perfection of a method which will absolutely immobilize the spine throughout the diseased area and make development of deformity impossible. The writer has done an operation for stiffening the knee joint¹ . . .", which "led to the conception if the periosteum of the spinous processes was carefully removed, and the processes were divided at their bases, and placed longitudinally in the interspinous space touching with either end the base from which the processes were removed and then the periosteum brought back and sutured, a similar condition would be produced."² On January 9, 1911, after preliminary work on the cadaver, with the assistance and encouragement of George Huntington, of the Department of Anatomy of Columbia University, Hibbs performed the first spinal fusion on a living subject, a boy with tuberculosis of the spine. The

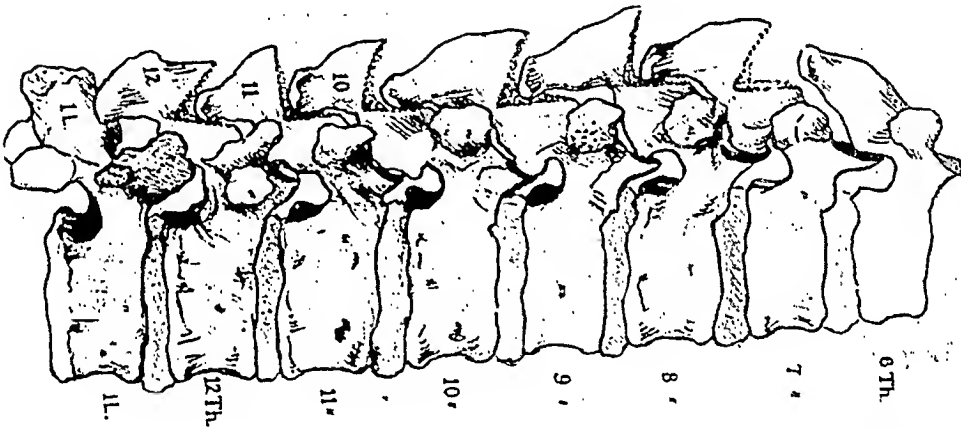
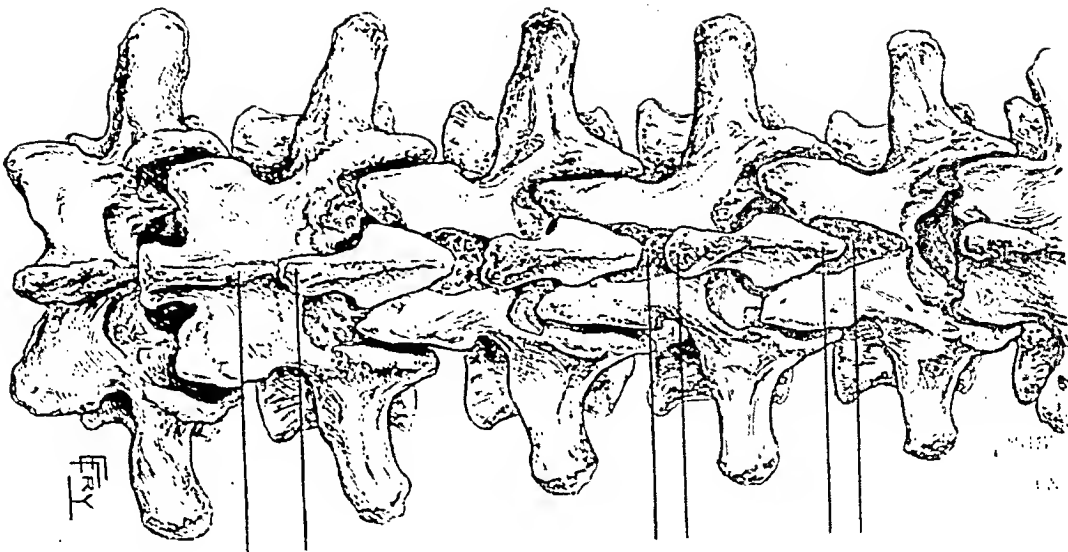


Fig. 1.—A. Original illustration used by R. A. Hibbs² in describing the first fusion operation (May, 1911). B. Illustration used in description of the operation including the use of clips from the lamina^{1,2} (May, 1912). C. Hibbs's illustration showing extended use of the fragments from the laminae and curettage of the lateral articulations (January, 1924).

patient recovered from the operation without complication, bony ankylosis occurred, and, over a period of months, the tuberculous lesion healed. Hibbs reported the operation on this and two other patients on May 27, 1911—"An Operation for Progressive Spinal Deformities²" (Fig. 1A). In this report he added: ". . . In the very young, however, I think it will be necessary to graft bone from the leg. This is a perfectly practical procedure." Further, ". . . No case of lateral curvature has yet been done, but I propose to do exactly the same operation, and if it is not sufficient, to do an arthrodesis between the lateral processes.² We see from these quotations how complete was Hibbs' conception of the principles involved.

In September of the same year, Albee³ reported three cases which he had treated in June and July by the use of a tibial graft implanted in the spinous processes. He stated: ". . . Previous to the herein reported cases, five patients were operated on and three or four spinous processes were split . . . and the tip of the lower half of the superior vertebra was then brought into approximation with the tip of the superior half of the next lower vertebra after green-stick fractures of each, and fastened with heavy kangaroo tendon. Chips of bone from the spinous processes were then placed in between so as to insure further bone union between these vertebrae. This union has been satisfactory so far as can be ascertained, but on account of its uncertainty and the large amount of cartilage in the vertebrae of small children, with its slowness of union and early lack of support, it has seemed best to devise a procedure which would be possibly more reliable and also give support from the beginning. These requirements can be fulfilled in no other way except by a strong bone graft. The different sources from which to secure a strong bone graft for an internal splint, which would give immediate support to the spine, were considered, and the crest of the tibia was selected as by far the most desirable and accessible."

Hibbs^{4, 4a} operated upon 43 cases with tuberculosis of the spine in the first year. These cases were reported in April, 1912 (Fig. 1B), and at this time Hibbs mentioned an extension of the operative procedure, stating that: "The space between the laminae is bridged by elevating a small piece of bone from the edge of the lamina, and placing it transversely across, its free end in contact with the lamina next below, with the gap between the spinous processes filled by their transposition. This makes me doubt the necessity for suturing the periosteum as I think bone becomes continuous and that a fusion takes place of the vertebrae operated upon." He emphasized here the complete subperiosteal dissection of the spinous processes and laminae as far laterally as the bases of the transverse processes. He further mentions suturing the periosteum of the spinous processes together on each side to close the gap produced by the interspinous ligament but questions the necessity for this step. Farrell⁵ reported many additional cases in January, 1915.

In June, 1917, Hibbs⁶ reported eight cases in which the spinal fusion was used in scoliosis for the prevention of increasing deformity and improvement in the stability of the spine. The first of these operations was performed in 1914. We note here the application of the suggestion made by Hibbs, in 1911, regarding the treatment of the lateral articulations: "The first thing to be done is to curet the lateral articulations which lie at the base of the transverse processes and are easily reached in children and in most adults."

In June, 1918, Hibbs⁷ reported 210 cases of spinal tuberculosis treated by the fusion operation, at which time he emphasized the use of special gauze packings to prevent bleeding and secure a clear field. Also, he pointed out that in the lumbar spine it was often desirable to split the spinous processes, turning portions of it upward and other portions downward, interdigitating these fragments. Fifty-nine fusion operations for scoliosis were reported^{7a} in January, 1924, and the further development of the operation described (Fig. 1C). Thus we have the picture of the development of the fusion to include not only the spinous processes, but the laminae and lateral articulations, resulting in a solid mass of thick bone extending completely across the posterior surface of the spinal column.

This early period should not be dismissed without mention of several other attempts at internal fixation of the spine. Hadra,⁸ in 1891, had wired together the spinous processes in treating fracture. Lange,⁹ in 1902, had begun to use steel rods sutured in the angles between the spinous processes and the laminae, and subsequently he used celluloid cylinders in a similar manner. Reporting his early work at the meeting of the American Orthopedic Association in 1910, he stated: "We must work for two things in our treatment of these cases; first, we must put our braces under the skin, and second, we must shorten the time for recovery for our patients." DeQuervain and Hoessly,¹⁰ in December, 1911, independently of a knowledge of Albee's work, reported the use of the spine of the scapula as a free graft into the split spinous processes. At the same time they reported an interesting series of experiments on dogs. Gallie,¹¹ in 1915, attempted arthrodesis by use of prepared beef bone grafts.

Despite the several technics described, this early period was marked not so much by study of the technic of spinal fusion, as by discussion as to whether spinal fusion was justified at all. As the operation was usually undertaken upon children, the possibility of interference with growth of the spine had to be considered as well as that of production of deformity by fusing only the posterior elements of the spine. Some orthopedists feared that fusion would stop the growth entirely, while others said that the vertebral bodies would continue to grow, while the fused posterior portion of the spine would remain stationary. The latter course would have been a desirable outcome in cases of tuberculosis as it would have caused the correction of the kyphosis, but unfortunately this did not occur. It was found, over a period of years, that growth of the spine continued at the

normal rate after fusion, and that the trunk-leg ratio remained the same in these patients as in normal individuals, allowing for the effect of the kyphos. No one knew whether the spines of very young children could be fused. This doubt was probably due to failure to realize that the spinous processes and laminae are ossified, even in the infant, although the lateral articulations and tips of the spinous processes are largely cartilaginous. The young spines did fuse, however, and a successful fusion was accomplished on one infant at the age of eleven months, probably the youngest ever attempted. Fusions were undertaken also for patients past the age of 60, again, with success.

The presence of tuberculosis in and around the laminae and articular processes presented another problem. The bone chips often failed to unite in the diseased area, and at times were even extruded, and sinuses developed, while the disease continued to advance. Furthermore, many of the patients of that day, long sufferers, with marked deformities, had developed amyloid disease, chronic sinuses, spastic paralysis or complications which produced an unfavorable general or local situation.

Many orthopedists feared that the traumatism of operation would stir up the disease and result in its spread as miliary tuberculosis or tuberculous meningitis. It was found, however, that the incidence of these complications was far less during the months following operation than it had been in the patients treated without operation. The operative mortality in the first 20 years of the operation was only 1.4 per cent, whereas 15 per cent of the patients died of pre-existing tuberculosis elsewhere in the body.

MODIFICATIONS

The second period in the evolution of spinal fusion may be characterized as one of modification. Perhaps the low mortality in cases described by Hibbs led to the impression that the operation was so simple that it could be learned through reading its description, or merely seeing it performed once. Lack of familiarity with the operation or lack of skill in its performance resulted in a high percentage of failure in the hands of some orthopedists, as a result of which the operation itself was in some quarters unqualifiedly condemned. Many of those who did not condemn or cease to employ the operation, sought to modify it for the sake of simplicity and reduction of the operative risk in their hands. The portion of the operation which seemed to give the most difficulty was the approach to and treatment of the lateral articulations. Forbes,¹² in 1920, omitting the inclusion of the lateral articulations in the fusion, split each spinous process and lamina into several fragments instead of two or three as Hibbs had been doing. Radulesco,¹³ in 1921, reported a modification of the Albee procedure, in which half a rib, with periosteum attached, was used instead of a tibial graft. Brown,¹⁴ and also Kleinberg,¹⁵ in 1922, reported the use of beef bone grafts along with a partial fusion operation. Thomas,¹⁶ in November, 1923, reported

the use of an osteoperiosteal graft and what he described as "wafer chips." Several operations extended the procedure beyond the posterior elements of the spine. Led by MacClennan,¹⁷ who resected a portion of the vertebral body for scoliosis, in 1922, and Royle,¹⁸ who removed a hemivertebra in 1928, Ito¹⁹ inserted bone grafts into slots in the vertebral bodies and reported a number of cases in 1934. Schede,²⁰ in 1925, used a graft as a prop between the ilium and transverse processes and props have even been used between the ilium and the ribs.

Most of these modifications were unnecessary, and some added an unjustifiable risk to the operation. The significant thing is that the spine was being fused. It matters not so much how a particular chip is laid or from whence a particular fragment of bone comes, but as to whether fusion is obtained, how quickly, and how strong.

APPLICATION TO OTHER CONDITIONS

A further development marked this second period—the application of the fusion to other conditions than tuberculosis and scoliosis. Hibbs,²¹ in 1922, reported the use of the fusion in 22 cases of "fracture-dislocation of the spine," the cases dating from 1916. The first one of the series was an unrecognized instance of spondylolisthesis, and represents the first application of the procedure to this anomaly. At least eight additional cases in this group had spondylolisthesis, but there were also cases of compression fracture of the spine. The operation was also applied to the other lumbosacral anomalies,²² such as the acute lumbosacral angle, posterior displacement of the fifth lumbar vertebra, transitional lumbosacral joints, and deformities of the lateral articulations. The first lumbosacral fusion for a mechanical condition was performed in October, 1914. It has also been employed in cases of round back, hemivertebra,²³ with or without partial resection, osteomyelitis,²⁴ occasionally in localized osteo-arthritis of traumatic origin, and, rarely, in other conditions. We have been doing the fusion in conjunction with removal of the ruptured nucleus pulposus since November, 1937.

OPERATIVE TECHNIC

The principle of the Hibbs operation has remained the same, but there have been several useful minor modifications. Hibbs devised a rasp which was driven into the lateral articulation for the purpose of scraping out the articular cartilage. It was found that even the rasp and curet usually did not effectively bare the articular surfaces. At the present time the articular cartilage with a little of the underlying cortical bone is removed with a straight osteotome or one especially angled for the purpose. Usually, the spinous process is removed and cut into long thin fragments which are eventually laid across the interlaminal spaces. If there is not sufficient bone at the site, as in some cases of spondylolisthesis or spina bifida, additional bone may be secured by removing neighboring spinous processes, or from the

region of the posterior superior iliac spine. The present procedure is, in general, as follows: A midline incision is made through the skin and subcutaneous tissue, and skin towels are applied with Michel clips. The deep fascia and supraspinous ligament are incised, and, with a Kermison elevator, the ligament is stripped from the tip of the spinous processes. The interspinous ligaments are incised longitudinally. The periosteum is carefully

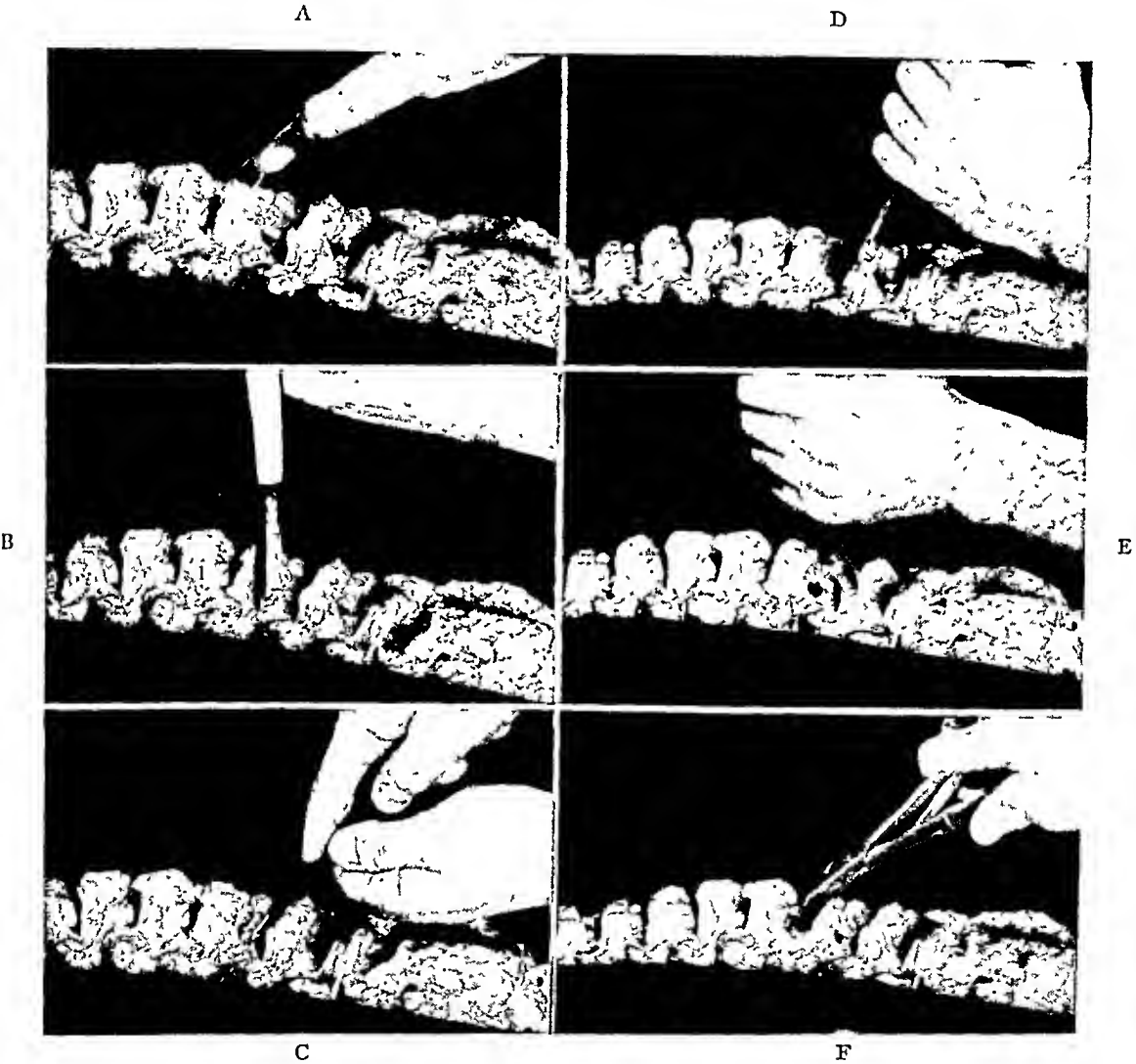


FIG. 2.—Technic of Spinal Fusion: A. Elevation of periosteum from spinous processes and laminae with Kermison and sharp, curved elevators. B. Completion of subperiosteal dissection and stripping of posterior capsules with "chisel" elevator. C. Dissection of interspinous ligament and stripping two-thirds of ligamentum flavum with curets, baring margins of the laminae and spinous processes. D. Excision of articular cartilage and subjacent cortical bone with straight or angled osteotome. E. Gouging of chips, into articular gap, subjacent fossae, and interlaminar spaces. The operation is completed by turning or placing the fragments from the spinous processes longitudinally from lamina to lamina. F. Removal of spinous processes. (This step is done in various ways and at various periods by different operators.)

stripped with sharp periosteal elevators from the spinous processes and laminae, far enough laterally to completely expose the lateral articulations (Fig. 2, A to F). This exposure is sharply limited, however, as there are usually blood vessels just beyond the lateral articulations which may be troublesome if opened. Further dissection may often be simplified by removal of



FIG. 3.—Specimens showing successive stages of the spinal fusion operation. A. Thoracic Spine. Subperiosteal dissection of spinous processes and laminae, excision of interspinous ligaments and ligamentum flavum; excision of posterior articular capsules; excision of articular cartilage, insertion of bare chips in articular gap; chips turned across interlaminar spaces from laminae and spinous processes. B. Lumbar Spine. The same, showing also the spinous processes cut into several fragments and placed across the lumbosacral joint, on the right.

the spinous processes at this stage. An assistant can be detailed to cut them into proper fragments or they may be split longitudinally before their removal. Next, the ligamentum flavum is largely removed, leaving only a thin anterior layer. This may be done very simply with a sharp curet by cutting its attachment to the superior margin of the distal lamina, then cutting it from the inferior margin of the proximal lamina, which overhangs it, and peeling it away from its most anterior layer. It is quite important to carefully remove all the ligament from the little fossa subjacent to each lateral articulation. The articulation is then denuded of cartilage and cortical bone with

osteotome and curet, with particular care to include all of the articular surface in the cup-shaped or oblique articulations, but to avoid penetration of the instruments or fragments of cartilage into the intervertebral foramen. A small fragment of bone is turned up with a gouge and jammed into the gap between the articular processes, and the whole fossa is bared of cortical bone by gouging up successive small chips which are locked together to form a small compact mass filling the fossa. Some operators prefer simply to insert a fragment of bone from the spinous process into the interarticular gap and do not thoroughly denude the articular cartilage or the fossa, which we consider the most crucial point in the fusion. Next, chips are cut with the gouge from the laminae and turned across the interlaminar spaces, interdigitating, and left attached at their bases as much as possible. Then the longer fragments from the spinous processes are laid longitudinally across the interlaminar space (Fig. 3 A and B). If the chips are simply dumped in like jackstraws, to lie in any direction and any location, the chances of pseudarthrosis are greatly increased. The careful placement of these chips is of greatest importance.

Finally, closure is made carefully and in anatomic layers. The periosteum and muscles are snugly sutured over the chips so as to obliterate any potential dead space, which might permit a large hematoma and allow displacement of the chips. The interspinous and supraspinous ligaments are then sutured, and finally the fascia and subcutaneous tissue, and the skin.

POSTOPERATIVE CARE

The postoperative care depends somewhat upon the condition for which the operation is undertaken. The general care of the patient is important, including adequate calcium and phosphorus, vitamins, and transfusions or iron if anemia is present. The chief feature of postoperative care is proper immobilization of the spine by bed rest and a brace or plaster jacket until the fusion has become sufficiently strong to support the weight of the trunk, and ordinary body movements. The patient is placed on a bed with a firm mattress and fracture board. Those with scoliosis are operated upon through a fenestrated plaster jacket, and the jacket is then reinforced. Other cases have a Taylor brace applied. Turning by the nurse is permitted, on the side, prone or supine, usually on a four-hour schedule. The patient is turned in such a way as to move the trunk *en masse*. Patients with a simple lumbosacral anomaly or compression fracture are kept in bed for about six weeks and wear the brace for a total of four months. Patients with spondylo-listhesis, scoliosis, or tuberculosis remain in bed about 12 weeks. Those with scoliosis wear a jacket for an additional three to six months, while the others wear a brace for a somewhat shorter period. These patients return to their regular activities within three months to one year following operation, depending upon the original condition, the progress of the fusion, and the character of the patient's activities.

COMPLICATIONS

It is to be expected that there will be an occasional failure of fusion, just as there are failures of union in the treatment of fractures, in osteotomies, and in bone grafts. However, these failures should be minimal and it should be realized and admitted that if they represent any appreciable percentage of the total number of cases, they must be ascribed to the technic of the operation and the postoperative immobilization. For example, during the five years 1931 to 1935, inclusive, more than 600 spinal fusions were done for all causes at the New York Orthopaedic Hospital. These operations were performed by the House Staff, Fellows, and Attending Surgeons. One or more psuedo-arthroses occurred in 14 per cent of the cases, nearly all of which were subsequently repaired. The largest number of failures, 18 per cent, was found in the group of spondylolistheses, while the lumbosacral fusions failed in only eight per cent, and in the fracture cases—none. It has been repeatedly demonstrated by clinical examination and roentgenograms, by subsequent operations, and occasionally by necropsy, that fusion can be accomplished in a large percentage of cases. It is futile, at the present time, to ascribe failures to the patient's "refusal to grow bone," or to the character of the operation. The operative mortality in more than 3,000 fusions at the New York Orthopaedic Hospital during the period 1911 through 1937 has been 0.6 per cent, whereas there has been no death from the operation since March, 1935. Thus, it is seen that the operation need not carry an appreciable risk to the life of the patient.

INDICATIONS

The indications for the operation may be summarized as follows, assuming a surgeon capable of properly performing the operation and an institution suitable for the care of the patient:

1. Tuberculosis: The treatment of choice at all ages, unless complete spontaneous natural fusion can be demonstrated, or the general condition of the patient or complications preclude the operation.
2. Scoliosis: In children with rapidly progressive deformity, or deformity with decompensation which can be corrected sufficiently to warrant fixation; in adults, occasionally for relief of pain.
3. Spondylolisthesis: All cases in the lower lumbar region unless contraindicated by age or the general condition of the patient.
4. Other lumbosacral anomalies: Pain of long duration, of moderate or great intensity, frankly due to the anomaly and unrelieved by other treatment.
5. Rupture of nucleus pulposus: Many of these joints are unstable primarily, and should be fused upon removal of the nucleus, preferably without laminectomy.
6. Compression fracture of the spine and some dislocations: As a means of maintaining reduction, hastening convalescence, and preventing pain.

7. With laminectomy: When indicated with a coincident orthopedic condition, or an extensive procedure.

8. Special indications in certain other conditions.

CONCLUSIONS

The effects of the operation should be clearly understood. A fusion may hasten and assure healing of tuberculosis and perhaps sometimes other infections, by completely immobilizing the diseased section of the spine. Progressive deformity due to tuberculosis, scoliosis, and spondylolisthesis may be prevented. The establishment of fusion for this purpose in cases of round back or hemivertebrae is open to question. In scoliosis and fracture, fusion may be the best or only means of maintaining correction of deformity. We do not attempt, and advise against, attempting to correct the deformity in tuberculosis. Fusion may be used for the relief of pain in the lumbosacral anomalies as well as all of the conditions just named. In many cases it may not only aid in the cure of the disease, the arrest or correction of deformity, and the relief of pain, but may be the quickest and most economical method of relief, in this way offering a financial advantage to both patient, hospital, and community. Thus, we see that spinal fusion has evolved during the past 30 years from a "radical" procedure in the treatment of tuberculosis, to a well established operation employed for a number of abnormalities of the spine. It is not a panacea, but in properly selected cases, and in skilled hands, fusion offers little risk and the possibility of great benefit to a large number of patients.

REFERENCES

- ¹ Hibbs, R. A.: An Operation for Stiffening the Knee Joint. *ANNALS OF SURGERY*, 53, 404, March, 1911.
- ² Hibbs, R. A.: An Operation for Progressive Spinal Deformities. *N. Y. Med. Jour.*, 93, 1013, May 27, 1911.
- ³ Albee, F. H.: Transplantation of a Portion of the Tibia into the Spine for Pott's Disease. *J. A. M. A.*, 57, 885, September 9, 1911.
- ⁴ Hibbs, R. A.: An Operation for Pott's Disease of the Spine. *J. A. M. A.*, 59, 433, August 10, 1912. Also, *N. Y. State Jour. of Med.*, 12, 501, September, 1912.
- ^{4a} Hibbs, R. A.: A Further Consideration of an Operation for Pott's Disease of the Spine. *ANNALS OF SURGERY*, 55, 682, May, 1912.
- ⁵ Farrell, B. P.: Hibbs' Osteoplastic Operation for Pott's Disease. *J. A. M. A.*, 64, 398, January 30, 1915.
- ⁶ Hibbs, R. A.: Treatment of Deformities of the Spine Caused by Poliomyelitis. *J. A. M. A.*, 69, 787, September 8, 1917.
- ⁷ Hibbs, R. A.: Treatment of Vertebral Tuberculosis by the Fusion Operation: Report of 210 Cases. *J. A. M. A.*, 71, 1372, October 26, 1918.
- ^{7a} Hibbs, R. A.: A Report of 59 Cases of Scoliosis Treated by the Fusion Operation. *Jour. Bone and Joint Surg.*, 6, 3, January, 1924.
- ⁸ Hadra, B.: Wiring of the Vertebrae as a Means of Immobilization in Fracture and Pott's Disease. *Am. Orthop. Assn. Trans.*, 4, 206, 1891. Also: *Med. Times and Reg.*, May 23, 1891.
- ⁹ Lange, F.: Support for the Spondylitic Spine by Means of Buried Steel Bars At-

- tached to the Vertebrae. *Am. Jour. Ortho. Surg.*, 8, 344, November, 1910.
- ¹⁰ Quervain, F. de, and Hoessly, H.: Operative Immobilization of the Spine. *Surg., Gynec. and Obst.*, 24, 428, April, 1917.
- ¹¹ Gallie, W. E.: Use of Boiled Bone in Operative Surgery. *Jour. Orthop. Surg.*, 16, 373, June, 1918.
- ¹² Forbes, A. M.: Technique of an Operation for Spinal Fusion as Practiced in Montreal. *Jour. Orthop. Surg.*, 2, 509, September, 1920.
- ¹³ Radulesco, A. D.: Bone Implants in the Spine. *Presse Med.*, 29, 284, April 9, 1921.
- ¹⁴ Brown, L. T.: Beef Bone in Stabilizing Operations of the Spine. *Jour. Bone and Joint Surg.*, 4, 711, October, 1922.
- ¹⁵ Kleinberg, S.: Unilateral Spine Fusion. *Arch. Surg.*, 26, 1035, June, 1933.
- ¹⁶ Thomas, H. B.: Fusion in Scoliosis. *J. A. M. A.*, 81, 1575, November 10, 1923.
- ¹⁷ MacLennan, A.: Scoliosis. *Brit. Med. Journ.*, 2, 864, November 4, 1922.
- ¹⁸ Royle, N. D.: The Operative Removal of an Accessory Vertebra. *Med. Jour. Australia*, 1, 467, 1928.
- ¹⁹ Ito, H., Tsuchiya, Y., and Asami, G.: A New Radical Operation for Pott's Disease. *Jour. Bone and Joint Surg.*, 16, 499, July, 1934.
- ²⁰ Schede, F.: Die Operation der Skoliose. *Ztschr. f. orthop. Chir.*, 46, 79, 1925.
- ²¹ Hibbs, R. A.: Fracture-Dislocation of the Spine Treated by Fusion. *Arch. Surg.*, 6, 598, May, 1922.
- ²² Hibbs, R. A., and Swift, W. E.: Developmental Abnormalities at the Lumbosacral Junction Causing Pain and Disability. *Surg., Gynec. and Obst.*, 48, 604, 1929.
- ²³ Smith, A. DeF., and von Lackum, H. L.: Removal of Vertebral Bodies in the Treatment of Scoliosis. *Surg., Gynec. and Obst.*, 57, 250, 1933.
- ²⁴ Smith, A. DeF.: A Benign Form of Osteomyelitis of the Spine. *J. A. M. A.*, 101, 335, July 29, 1933.

STENOSING TENDOVAGINITIS AT THE RADIAL STYLOID (DEQUERVAIN'S DISEASE)

PHILIP C. POTTER, M.D.

NEW YORK, N. Y.

THE PURPOSE OF THIS PAPER is to call attention to the existence of a relatively common and extremely disabling condition, first described in 1895 by Fritz DeQuervain. My interest was aroused when, some five years ago, I encountered my first case of stenosing tendovaginitis at the radial styloid. In speaking to other surgeons of this condition I have been surprised to find that many were unaware of its existence. No credit is claimed for original observations, but it is felt that a useful purpose can be served by once again presenting the facts and thereby drawing attention to a disease entity which it seems is frequently overlooked.

DeQuervain's original article,¹ paints the picture so clearly that I shall quote from it at some length: "Although chronic disease involving tendon sheaths is most frequently construed as tuberculosis, there are types which neither from the clinical picture nor from the anatomic findings should be placed in this category. Among these may be mentioned tendovaginitis chronica sicca, tendovaginitis prolifera urica, and serous nontuberculous tendovaginitis. Chronic nontuberculous tendovaginitis has seldom called for surgical intervention, and is mentioned in most textbooks briefly, if at all. It, therefore, seems proper to discuss a condition which, although still belonging to the first type, tendovaginitis sicca, deviates in some important respects from the exact picture and in which surgical treatment has proved extremely beneficial. Through the kindness of Dr. Theodor Kocher I was given the opportunity to observe and to operate upon my first case when I was his assistant in the Surgical Clinic in Bern. Frau L., who occupied herself with housekeeping and woodgathering, noticed, in October, 1893, that the moving of her right thumb had gradually become painful. The pain was localized chiefly over the distal end of the radius and radiated up the forearm. The pain was sometimes so severe that she was unable to make grasping motions. There had been no swelling or other signs of inflammation. Despite massage with spirits of camphor and the application of heat, the pain had increased so that, in February, 1894, she came to the Surgical Clinic. The findings at her first visit were as follows: There was no sign of tuberculosis, syphilis or gout in the entire body. Motion of the right thumb was painful. Palpation revealed a slight thickening over the common sheath of the extensor pollicis brevis and abductor longus muscles. This sheath was keenly sensitive to pressure. There was no crepitation. It appeared that the condition might well result from a thickening of the sheath of the extensor pollicis brevis and abductor longus tendons, firmly encased as it is by the fibers of the dorsal carpal ligament, and that the functional

disturbances were due to increased friction in this region. Assuming a stenosis of the sheath, on March 7, 1894, under cocaine anesthesia, I removed the common sheath of the extensor brevis pollicis and abductor longus. The sheath was slightly thickened. Otherwise it appeared normal, as did the bone. Following operation there was no further pain and full use of the thumb returned in a few days. A report, March 7, 1895, stated that the patient had remained completely cured." DeQuervain described four similar cases, all promptly relieved by operation.

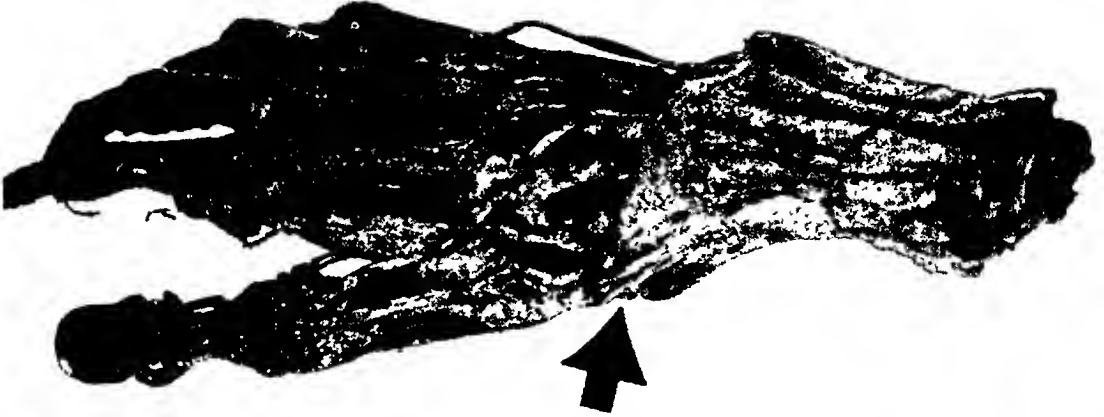


FIG. 1.—Shows the tendons of the abductor longus and extensor brevis pollicis passing upward beneath the dorsal carpal ligament. It is this portion of the ligament which is divided at operation.

DeQuervain's disease first appeared in American literature in 1927, in an article by Stein.² He reported five cases and described a similar condition involving the tendon of the extensor carpi ulnaris which passes through the fifth radial compartment. In 1928, Schneider³ reported 15 cases of his own, and referred to an article by Alfons Eschle, of Basle, who, in 1924, collected 110 cases from the foreign literature, to which he added 19 personal cases. In 133 of these cases, where the sex was known, there were 119 females and 14 males. In 1930, Finkelstein⁴ reviewed the subject thoroughly and added 32 cases from the Hospital for Joint Diseases. In 1935, W. M. Brown⁵ reported the first case to appear in the British literature. This patient was cured after 18 weeks in plaster. This was followed, in 1936 by an article by Burns and Ellis⁶ in the *Lancet*. They reported 28 personal cases. In the same year, Patterson⁷ reported six cases from the Bridgeport Hospital. In 1938, Keyes⁸ read an excellent paper before the Surgical Section of the New York Academy of Medicine. He reported one personal case, and referred to a second, a patient of another surgeon. This was an anesthetist who contracted the disease in his left hand as the result of gripping an ether mask for long periods of time. He continued his work while under treatment and within a short time the right hand became involved. In 1938, an article by Cotton, Morrison and Bradford⁹ appeared, and in the following year a report by Diack and Trommald.¹⁰ In 1941, C. F. Wood¹¹ stated that in a careful review of the literature he had been able to find 250 cases reported up to the year 1938. Inasmuch as some

confusion exists in regard to so-called "snapping finger" (*doigt à ressort*) and true stenosing tendovaginitis, I shall include two excellent references which fully describe the former condition—Compere,¹² and Zelle and Schnepf.¹³

The tendons of the abductor longus and extensor brevis pollicis pass through a shallow groove on the outer surface of the styloid process of the radius. The tendons at this point have a definite sheath which is in close contact with the dense fibers of the dorsal carpal ligament (Fig. 1). If the interphalangeal joint is flexed and the thumb actively abducted and

drawn toward the ulnar side it will be noted that the tendons of the abductor longus and extensor brevis pollicis, while lying parallel in the groove of the radius, thereafter promptly diverge toward their insertions, the base of the metacarpal and the base of the proximal phalanx of the thumb respectively (Fig. 2). It will likewise be noted that in full abduction these tendons exert a considerable pull on the distal end of the radial compartment, and that the direction of this pull is at right angles to the long axis of this compartment. The

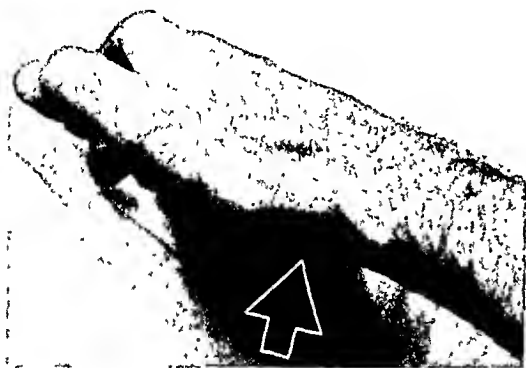


FIG. 2.—Shows the tendons of the abductor longus and extensor brevis pollicis. It will be seen that these tendons come together at an angle to pass upward beneath the ligament.

tendon sheath is thus squeezed between the dorsal surfaces of the tendons and the dorsal ligament.

The exciting cause may be acute trauma. More frequently DeQuervain's disease is the result of sustained or oft repeated active adduction from a position of the extreme abduction.* The pathology found at operation varies. Most authors agree that there is a thickening of the sheath and of the overlying dorsal ligament, with a resulting constriction of the tendons. In some cases there have been signs of inflammation, as evidenced by the presence of fluid within the sheath and by a roughening of the tendon surfaces. In the writer's cases the outstanding finding was a marked thickening of that portion of the dorsal carpal ligament which overlies the sheath. This thickening decreased the diameter of the canal to such a degree as to interfere with the smooth action of the enclosed tendons. In one case there was a localized thickening of the ligament which had resulted in an hour-glass deformity of the tendons. It is possible that the primary pathology may well be limited to the dorsal ligament and that the variations from the normal which are encountered in the sheath and tendons are secondary to this. Sections

* Although the writer has not seen a report of stenosing tendovaginitis resulting from the operation of firearms, the causative factor is present in the handling of a gun over a prolonged period of time.

of excised ligaments have shown dense fibrous tissue with sometimes a mild degree of round cell infiltration.

The diagnosis is not difficult. The chief complaint is pain on moving the thumb. There is often a definite history of chronic trauma—bottle corking, piano playing, crocheting, boxing, and, in one of my cases, the holding of an artist's palette for hours at a time. There may or may not



FIG. 3.—Shows deformity of right wrist caused by thickening of the dorsal carpal ligament. This is not a constant finding.

be discernible swelling in the region of the canal (Fig. 3). There is acute tenderness over the radial styloid. An excellent diagnostic sign, as pointed out by Finkelstein, is the following: The patient's thumb is placed in the hollow of the palm and grasped by the remaining fingers (Fig. 4). With the hand in this position even slight forced ulnar deviation at the wrist will produce excruciating pain. Roentgenograms are universally negative. Under differential diagnosis must be mentioned old fracture of the carpal scaphoid, fibrinous tenosynovitis involving the sheath of the extensor longus pollicis, rheumatoid and gonorrheal arthritis, "snapping finger," and sprain of the internal lateral ligament of the wrist joint.

Treatment consists in longitudinal division of that portion of the dorsal carpal ligament which overlies the sheath. This will in all probability be sufficient. In some cases which have been reported it has seemed wise to excise portions of the ligament or the sheath, or both. A few cures following conservative treatment (plaster of paris for from 6 to 18 weeks) have been

reported. Many have been treated conservatively, to no avail, and have subsequently been operated upon.

The technic is as follows: Under novocain anesthesia, and with or without a tourniquet applied to the upper arm, a longitudinal incision, one and one-quarter inches in length, is made. The lower end of this incision corresponds to the proximal and radial angle of the anatomical snuff box, and



FIG. 4.—In stenosing tendovaginitis even slight, forced ulnar deviation with the hand in this position causes extreme pain

is continued upward just to the ulnar side of the tendon of the flexor brevis pollicis. A small branch of the radial nerve and a vein, which cross the line of incision, must be recognized and avoided. A transverse incision may be employed at the level of the styloid process. This will result in a less noticeable scar, but care must be taken not to injure the radial artery. The dorsal ligament lies directly beneath the subcutaneous fat and that portion which covers the sheath is easily recognized when the thumb is forcibly abducted. The ligament is divided from above downward. This may be done by inserting the point of a No. 11 Bard-Parker blade beneath the upper edge of the ligament and cutting distally with the sharp edge away from the tendons. The contents of the canal can now be examined and, if thought necessary, a portion of the ligament, sheath, or both, can be excised. The superficial fascia is closed with fine silk or plain catgut and the skin with interrupted fine silk. It has been my custom to apply a light

basswood splint to be left in place for two or three days. This not only minimizes discomfort, but hastens healing and is a safeguard against infection.

During the past five years I have operated upon eight cases of DeQuervain's disease, six at the Doctors' Hospital and two at Bellevue Hospital.

ABBREVIATED CASE REPORTS

Case 1.—Z. H. T. A woman, age 65. Duration of symptoms—six months. Causative factor—crocheting. Typical signs. X-ray negative. Operation May 25, 1937. Pathology—localized thickening of dorsal ligament at its center, producing hour-glass constriction of tendons at that point. Sheath thickened. Procedure—division of dorsal ligament.

Case 2.—J. H. A man, age 28. Duration of symptoms—three months. Causative factor—boxing. Typical signs. X-ray negative. Operation January 21, 1938. Pathology—thickening distal half of dorsal ligament. Slight thickening of sheath. Tendons normal. Procedure—division of dorsal ligament.

Case 3.—F. S. A woman, age 67. Duration of symptoms—three weeks. Causative factor—holding painter's palette for long periods of time. Typical signs. X-ray negative. Operation October 16, 1939. Pathology—diffuse thickening of dorsal ligament with thickening of sheath. Procedure—division of dorsal ligament.

Case 4.—L. P. A woman, age 38. Duration of symptoms—three months. Causative factor—undetermined. Typical signs. X-ray negative. Operation November 8, 1939. Pathology—diffuse thickening of dorsal ligament. Sheath thin-walled and contained a quantity of clear fluid. Tendons normal. Procedure—division of dorsal ligament.

Case 5.—A. G. A man, age 55. Duration of symptoms—one month. Causative factor—machine work. Typical signs. X-ray negative. Operation June 19, 1941. Pathology—diffuse thickening of dorsal ligament. Moderate amount of clear fluid in thickened sheath. Procedure—division of dorsal ligament.

Case 6.—G. A. A woman, age 50. Duration of symptoms—two months. Causative factor—housework. Typical signs with noticeable swelling over sheath. X-ray negative. Operation June 24, 1942. Pathology—diffuse thickening of dorsal ligament. Procedure—division of dorsal ligament. This patient is recovering slowly owing to an associated arthritis.

Case 7.—A. H. A woman, age 35. Duration of symptoms—seven months. Causative factor—stenography. Typical signs with noticeable swelling. X-ray negative. Operation July 31, 1942. Pathology—diffuse thickening of dorsal ligament with increased fluid within sheath. Procedure—division of dorsal ligament with excision of edges.

Case 8.—A. M. A nurse, age 30. Duration of symptoms—one week. Sudden pain developed in the process of drawing a sheet tightly across a bed. Typical signs. X-ray negative. The hand, wrist and forearm were immobilized for one month without benefit. Operation October 8, 1942. Pathology—moderate thickening of the dorsal ligament, thickening of sheath with excess fluid. Procedure—division of dorsal ligament.

CONCLUSIONS

DeQuervain's disease, or stenosing tendovaginitis at the radial styloid, is a relatively common but frequently overlooked condition. The symptomatology is definite. The surgical treatment is simple and uniformly successful. It is hoped by once again describing the outstanding characteristics of this disease that it will be more frequently recognized.

REFERENCES

- ¹ DeQuervain, Fritz: *Cor.-Bl.f. Schweiz. Aertzte*, 25, 389, 1895.
- ² Stein, H. C.: *Am. J. Surg.*, 3, 77, July, 1927.
- ³ Schneider, C. C.: *Surg. Gynec. Obst.*, 46, 846, June, 1928.
- ⁴ Finkelstein, H.: *J. Bone and Joint Surg.*, 12, 509, July, 1930.
- ⁵ Brown, W. M.: *Brit. Med. J.*, 2, 538, September 21, 1935.
- ⁶ Burns, B. H., and Ellis, V. H.: *Lancet*, 1, 717, March 28, 1936.
- ⁷ Patterson, D. C.: *N. E. J. Med.*, 214, 101, January 16, 1936.
- ⁸ Keyes, H. B.: *ANNALS OF SURGERY*, 107, 602, April, 1938.
- ⁹ Cotton, F. J., Morrison, G. M., and Bradford, C. H.: *N. E. Med. J.*, 219, 120, July 28, 1938.
- ¹⁰ Diack, A. W., and Trommald, J. P.: *West. J. Surg.*, 47, 629, November, 1939.
- ¹¹ Wood, C. F.: *South. Surg.*, 10, 105, February, 1941.
- ¹² Compere, E.: *ANNALS OF SURGERY*, 97, 773, 1933.
- ¹³ Zelle, O., and Schnepf, K.: *Am. J. Surg.*, 33, 321, August, 1936.

TRENDS IN GENERAL SURGERY

REVIEW OF FIVE YEARS SURGICAL EXPERIENCE AT HARPER HOSPITAL

M. J. THORSTAD, M.D., H. C. SALTZSTEIN, M.D.,

AND

A. D. McALPINE, M.D.

DETROIT, MICH.

FROM THE SURGICAL SERVICE, HARPER HOSPITAL, DR. A. D. McALPINE, SURGEON IN CHIEF, DETROIT, MICH.

HARPER HOSPITAL is a 600-bed general hospital of which approximately 250 beds are devoted to general surgery. There are 110 general surgeons on the hospital staff. Twelve surgeons perform two-thirds of all the major general surgery. This is preponderately a private institution as only ten beds are set aside for Staff general surgery, done by the resident surgeon under the supervision of an attending surgeon. Five beds are similarly assigned to Staff gynecology.

The present communication is a review of the total surgical statistics for the five-year period from 1937 to 1941. The aim is to present the average situation in a general hospital of this type, as indicating the risks in operations, and a few of the trends in general surgical practice. No attempt is made to present an exhaustive discussion of each group of surgical procedures.

A comparison of the total surgical admissions, the total major operations, and the operative mortality rates for the five-year period, is shown in Table I.

TABLE I
TOTAL OPERATIONS AND MORTALITY RATES

	1937	1938	1939	1940	1941
Surgical admissions.....	10,014	9,016	8,754	8,407	11,125
Major operations*.....	3,755	3,600	3,509	3,891	4,233
Operative deaths.....	178	98	110	108	128
Per cent operative mortality rate†.....	4.8%	2.7%	2.3%	2.8%	3.0%
Nonoperative deaths‡.....	93	82	59	66	68

*Major operations include the following surgical procedures: All abdominal operations, thyroidectomy, mastectomy (simple and radical), thoracic surgery, nephrectomy, herniorrhaphy, extensive perineal repair, prostatectomy (suprapubic and transurethral), repair of wound disruption, major orthopedic operations, amputation of extremities, mastoidectomy, Caldwell-Luc operations, radical frontal operations, and neurologic surgery.

The hospital practice is to list the following operations as *minor procedures*: Surgery of the eye, adenoidectomy, tonsilectomy, submucous resection, bronchoscopy, tracheotomy, biopsy, simple perineal repair, incision of abscess, diagnostic curettage, hemorrhoidectomy, polypectomy, fistulectomy, hydrocelectomy, epididymectomy, orchidectomy, dental surgery, suturing of tendons and lacerations, and closed reductions of fractures. These cases have not been included in the statistical data.

†During this five-year period the mortality rate for all major surgery has averaged approximately 3.2 per cent.

‡Nonoperative deaths include all deaths occurring on the Surgical Service upon whom no operation was performed. Of the 68 nonoperative deaths during 1941, two-thirds were due to carcinoma of various organs, brain tumors, sarcomata, Hodgkin's disease, and cirrhosis of the liver. The remainder of the deaths were the result of burns, uremia, cerebral apoplexy, ruptured kidney, leptomeningitis, skull fractures, fractures of femur, influenza, pneumonia, hemorrhage from intestinal tract, etc.

The autopsy rate for 1941 is low (Table II). There is a very concerted effort being made to raise the percentage rate for 1942. In a private hospital, the intern staff must receive the wholehearted support of the attending physicians to obtain permission for postmortem examinations.

TABLE II
AUTOPSY STATISTICS, 1941

	No. of Cases	Per Cent of Total Deaths
Total autopsies for 1941.....	170	34.5%
Surgical autopsies.....	83	42.0%
Medical autopsies.....	87	30.0%

SURGERY OF THE APPENDIX

During 1941 there were 1502 appendicectomies performed at Harper Hospital, *i.e.*, 35.5% of all major operations. This disease stands out as the most common condition for which surgical intervention is undertaken.

In Graph I we have attempted to show certain trends in the surgical aspects of appendicitis during the past five years. The following conclusions can be drawn:

(1) There has been an increase in the total number of appendicectomies performed during this period.

(2) The total mortality rate for appendicitis and its complications treated surgically has fallen to the low mortality rate of 0.3% in 1941, or five deaths in 1502 operations.

(3) In 1941 there were 41 operations for acute appendicitis, with either abscess or generalized peritonitis. There were no deaths among these patients. This indicates a very significant advance in the treatment of this disease.

(4) The number of cases of appendicitis, with peritonitis, submitted to surgery has increased while the number of patients with abscess formation has decreased. There is apparently a definite tendency toward earlier operation in ruptured appendicitis without waiting for a localization of the infection and abscess formation.

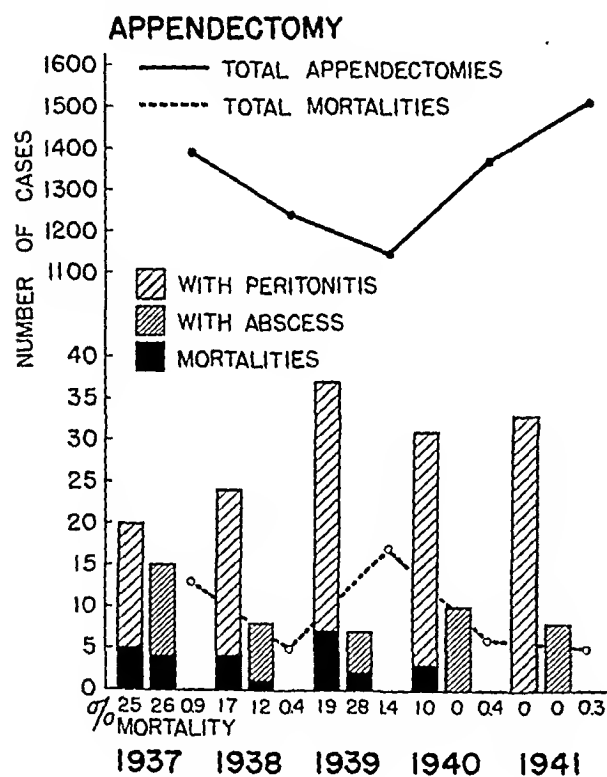
A more detailed analysis of the appendicectomies performed in 1941 is illustrated in Table III.

Analysis of the five deaths following appendicectomy during 1941 are listed as follows:

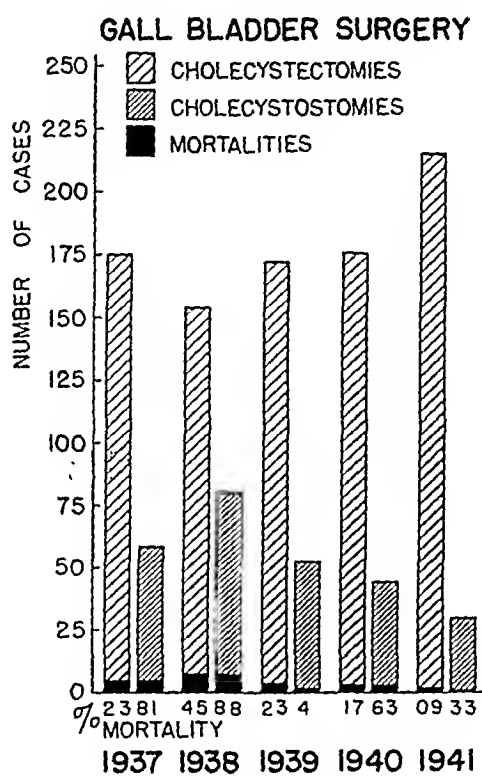
TABLE III
CLASSIFICATION OF APPENDICECTOMIES, 1941

	No. of Cases	Deaths
Acute uncomplicated appendicitis.....	240	0
Subacute appendicitis.....	40	0
Interval and chronic appendicitis.....	701	2
Acute appendicitis, with abscess.....	8	0
Acute appendicitis, with peritonitis.....	33	0
Carcinoid of appendix.....	1	0
Appendicectomy in conjunction with other operative procedures..	479	3
	<hr/> 1502	<hr/> 5....0.3%

a. Two deaths listed as chronic appendicitis: (1) An appendicectomy was performed on a 19-year-old white female, who was five months pregnant. She died 36 hours postoperatively from an acute massive bilateral pneumonia and pulmonary edema secondary to a weakened heart. No autopsy was obtained. *Pathologic Report*: Chronic catarrhal appendicitis. (2) A 52-year-old Polish male, who could speak no English, was admitted to Harper Hospital with generalized abdominal cramps, diarrhea, and nausea of nine days duration. An appendicectomy was performed in conjunction with severing of peritoneal bands at the terminal ileum. The patient died on the fifth postoperative day. Autopsy revealed an acute toxic hepatitis, cerebral congestion, and hemorrhage into the great mesentery. *Pathologic Report*: Chronic catarrhal appendicitis.



GRAPH I



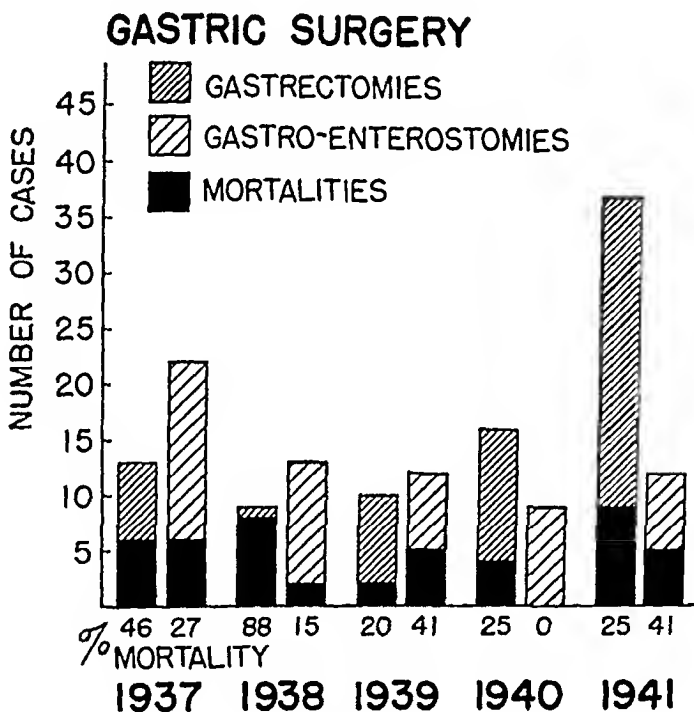
GRAPH II

b. Three deaths listed "Appendicectomy with other operations": (1) Cholecystectomy and appendicectomy were performed on a 36-year-old white female. She died 48 hours postoperatively of an extensive bilateral pneumonia, suggestive of an aspiration type and an old rheumatic heart disease. No autopsy was obtained. *Pathologic Report*: Chronic catarrhal appendicitis. (2) An appendicectomy was performed on a 71-year-old white male, in conjunction with a repair of a strangulated right inguinal hernia. The patient died on the twenty-ninth postoperative day of a probable pulmonary infarction, and arteriosclerotic heart disease. No autopsy was obtained. *Pathologic Report*: Chronic catarrhal appendicitis. (3) A transurethral prostatectomy was performed upon a 58-year-old white male. Three weeks later he developed acute abdominal symptoms, diagnosed as acute appendicitis.

Appendicectomy was performed, and the patient died 13 days postoperatively. Autopsy diagnosis was pulmonary edema and acute tubular nephrosis. *Pathologic Report*: Chronic catarrhal appendicitis.

In summarizing the causes of death in the above five patients none were due to intra-abdominal complications: The causes of death are listed below:

- (1) Massive pneumonia during pregnancy.
- (2) Toxic hepatitis.
- (3) Aspiration pneumonia (associated cholecystectomy).
- (4) Pulmonary infarction (associated strangulated hernia).
- (5) Pulmonary edema and acute tubular nephrosis (associated prostatectomy).



GRAPH III

SURGERY OF BILIARY TRACT

It is generally recognized that safe and successful surgery of diseases of the biliary tract requires mature judgment and much experience. In Graph II are depicted the trends and results of biliary surgery:

(1) There has been a decided increase in the number of cholecystectomies performed during the past few years. In 1941, 217 cholecystectomies were performed, with two deaths (0.9% mortality). One hundred ninety-three of these cases were for chronic cholecystitis.

(2) Cholecystostomy has had a steady decline in employment during the past five years. Thirty cholecystostomies were performed during 1941, with one death (3.3% mortality). Nineteen of these were for chronic and 11 for acute cholecystitis.

Data on the incidence of exploration of the common duct, drainage of

the common duct, and the incidence of jaundice were not obtained, but these complications are included in the above statistics.

SURGERY OF THE STOMACH AND SMALL INTESTINES

Though the number of gastrectomies is not large, there was a marked increase in 1941 (Graph III). Approximately two-thirds of these operations were for peptic ulcer and one-third for carcinoma of the stomach. The mortality rate for gastrectomy during the past three years has ranged from 20 to 25 per cent. The mortality rate for gastrectomy in the presence of peptic ulcer was 19 per cent for 1941, approximately the same as for carcinoma of the stomach. However, one surgeon performed 13 gastrectomies during 1941, with a mortality of 7.7 per cent. One of the authors (M.J.T.) performed ten gastrectomies in 1942 with no deaths.

There have been almost the same number of gastro-enterostomies performed each year, *i.e.*, 10 to 15 cases. Of the 11 gastro-enterostomies performed in 1941, five were for carcinoma and six for obstructing duodenal and pyloric peptic ulcers. The mortality (1941) was 41%. Death following gastro-enterostomy was caused by atelectasis, bronchopneumonia, difficulty with the stoma, ascites, and extension of the carcinoma of the stomach.

Gastrostomy is an uncommon operative procedure in Harper Hospital, there being only three such operations during 1941. Enterostomy has not been entirely replaced by the use of the Miller-Abbott tube. Eleven enterostomies were performed in 1941, with two deaths, an operative mortality rate of 18%.

The mortality from perforated peptic ulcer is difficult to analyze. However, one can say that the mortality rate for operative treatment of this complication of peptic ulcer during the past 11 years in Harper Hospital is over 20 per cent, and has shown no improvement during the past five years (Table IV).

TABLE IV
PERFORATED PEPTIC ULCERS

Year	Total No. of Cases	Nonoperative		Operative		
		Cases	Deaths	Cases	Deaths	% Mortality
1937.....	21	2	1	19	5	26.0%
1938.....	21	2	0	19	2	10.5%
1939.....	11	1	1	10	2	20.0%
1940.....	9	1	1	8	4	50.0%
1941.....	22	1	1	19	3	15.8%

Analysis of deaths from perforated peptic ulcer during 1938 to 1941 revealed:

(1) Three patients died without benefit of surgical intervention. Two of these had symptoms of perforation from 24 to 48 hours before admission, and both died within one day after admission to hospital. The third patient had been ill for three weeks with severe pain and increasing jaundice. Autopsy revealed an unsuspected perforated peptic ulcer of the duodenum involving

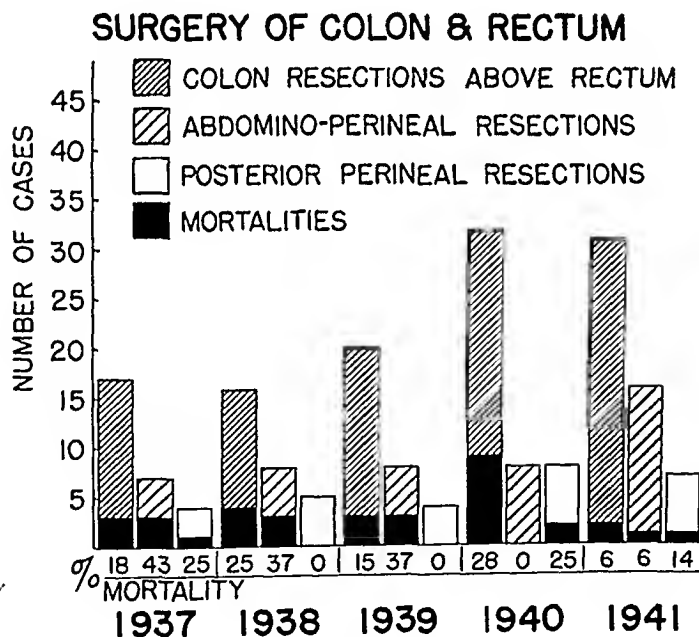
the liver and common duct. All of these patients entered the hospital in a moribund condition and failed to respond to preoperative treatment.

(2) Of 11 patients who died following operation, the duration of symptoms of perforation in six cases was less than eight hours. Four patients died of pulmonary complications, and two from extension of the peritonitis. The operations were uniformly performed under spinal anesthesia, and consisted of closure of the perforation with interrupted sutures and reinforcing with omental fat. One fatal case had had a previous operation for closure of perforated peptic ulcer four years before.

In summary it is noted that an occasional patient with perforated peptic ulcer recovers without operation; several still come in in moribund condition, too ill to undergo operation. Of the postoperative deaths, several came in within six to eight hours of the time of perforation.

SURGERY OF THE COLON AND RECTUM

The number of operations performed upon the colon and rectum shows a decided increase. Surgery of the large intestine may be divided into three groups, on an anatomic basis (Graph IV):



(1) There were 31 resections of the colon above the rectosigmoid, for cancer and gunshot wounds, with a mortality rate of 6.5%, during 1941. Most of the operations were performed by the modified Mikulicz technic.

(2) Abdomino-perineal resections of the rectum for adenocarcinoma increased from six operations, in 1940, to 16, in 1941. The mortality rate has fallen sharply during the last year; in 1941, 16 abdomino-perineal resections were performed, with one fatality, a 6% mortality.

(3) Seven perineal resections for selected cases of adenocarcinoma of

TRENDS IN GENERAL SURGERY

the lower portion of the rectum were performed in 1941, with a 14% mortality rate.

HYSTERECTOMY

From the five-year statistics concerning surgery of the uterus, (Graph V), the following conclusions can be drawn:

- (1) There has been a 50 per cent increase in the number of hysterectomies performed during the past four years.
- (2) From 1937 to 1941, the mortality rate ranged between one and two per cent. In 1941, it dropped to 0.6% (three deaths) in 496 cases. Siddal and Mack¹ reported the experience of Harper Hospital in hysterectomies for the five years, 1928 to 1932. For that period the mortality was 3.3%.
- (3) Of the hysterectomies performed, approximately one-half are performed by general surgeons and the other half by gynecologists.
- (4) Hysterectomies performed by general surgeons show a higher mortality, the five year rate being 2.16%, as against 0.83% for the gynecologists.

The various types of hysterectomies performed during 1941 are shown in Table V. Vaginal hysterectomy is performed chiefly by the gynecologists.

TABLE V
TYPES OF HYSTERECTOMIES, 1941

	General Surgery		Gynecology	
	Cases	Deaths	Cases	Deaths
Supravaginal hysterectomy.....	183	2	159	1
Total hysterectomy.....	73	0	66	0
Vaginal hysterectomy.....	2	0	13	0
	258	2	238	1

Siddal and Mack,¹ in their study, found the mortality rate for total hysterectomy to be twice as great as for supravaginal hysterectomy in the 1928-1932 period. However, in 1941 there were no deaths from total hysterectomy, and this operation was performed in 25 per cent of the cases. Records do not show whether total hysterectomy was employed oftener in the less complicated cases.

WOUND DISRUPTION

Each year there are a few complete abdominal wound eviscerations—(40 in the entire five-year period). Only cases taken to the operating room for resuture are included. The mortality rate for the five-year period has averaged 32 per cent (Table VI).

TABLE VI
WOUND DISRUPTIONS

	1937	1938	1939	1940	1941
Total cases.....	13	8	5	8	6
Fatal cases.....	5	2	1	3	2
Per cent mortality rate.....	31%	25%	20%	37%	33%

Hysterectomy accounts for 25 per cent of the wound disruptions; and cholecystectomy and appendicectomy 17 per cent each.

HERNIA

Types of herniotomies and deaths for each of the five years, 1937 to 1942, are listed in Table VIII. The highest mortality rate during this period was 1.3%, in 1937, and dropped to 0.4%, in 1941. There is an occasional death in each classification but the most regular death rate occurs in the small group of strangulated herniae.

SURGERY OF THYROID

Subtotal thyroidectomy is the most common type of operative procedure employed in the treatment of goiter. Only 33 multiple-stage operations were listed during the past five years.

TABLE VII

OPERATIONS FOLLOWED BY EVISCERATION

Hysterectomy.....	10
Cholecystectomy.....	7
Appendectomy.....	7
Carcinoma of viscera.....	5
Perforated peptic ulcer.....	3
Splenectomy.....	2
Colostomy.....	1
Acute pancreatitis.....	1
Epigastric hernioplasty.....	1
Intestinal obstruction.....	1
Subhepatic abscess.....	1
Perforated typhoid ulcer.....	1
No. of Cases.....	40

The mortality rate of thyroidectomy has been low for several years, the lowest being in 1941, when it was 0.7%, or three deaths in 286 cases (Graph VI).

During the past five years there have been nine cases of carcinoma of the thyroid.

The type of anesthetic agent used during thyroidectomy varied a great deal. Many surgeons use local novocain anesthesia and others gas-ether, with or without intratracheal intubation.

TABLE VIII

CLASSIFICATION OF HERNIOPLASTY

Types	Cases in	Deaths				
		1937	1938	1939	1940	1941
Uncomplicated inguinal hernioplasties.....	608	5	0	1	1	0
Strangulated inguinal hernioplasties.....	17	3	1	1	0	2
Femoral hernioplasties.....	26	0	0	2*	0	0
Umbilical hernioplasties.....	13	0	0	1	0	1
Ventral hernioplasties.....	45	1	0	1	1	0
	709	9	1	6	2	3

*The two deaths listed under femoral hernioplasty occurred in the presence of strangulation of the intestine.

MASTECTOMY

There were no deaths from mastectomy, either simple or radical, during the past five years.

A study of Graph VII reveals the following trends:

(1) The number of mastectomies is increasing. The increase is chiefly in the simple mastectomy, and indicates an increasing appreciation of the importance of removing benign lesions of the breast.

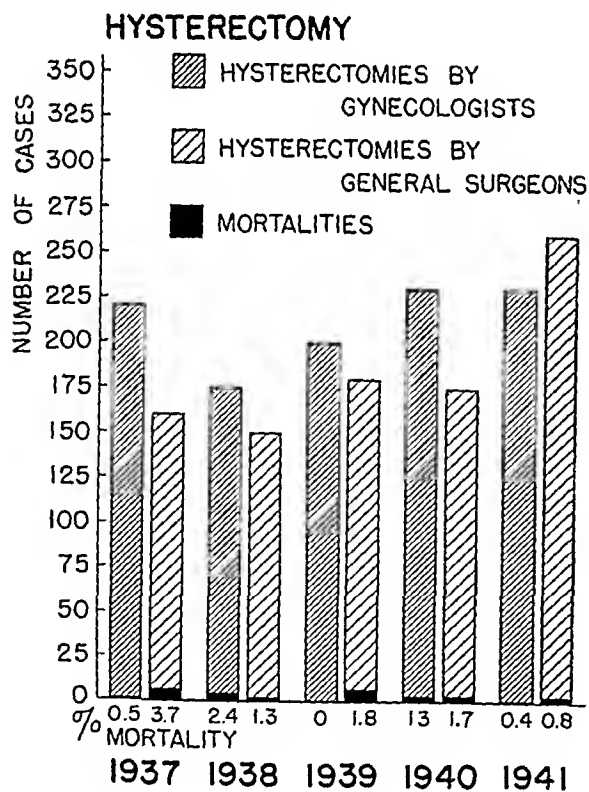
(2) The number of cases of carcinoma of the breast operated upon each year fluctuates, but is not increasing.

(3) Each year simple mastectomy is employed for less than ten cases of carcinoma. This is approximately 20 per cent of the total number of operations for cancer of the breast.

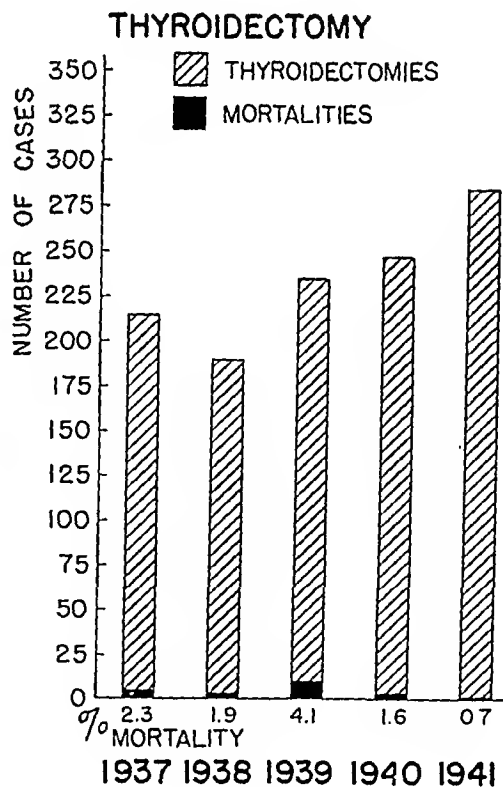
(4) Each year a few radical breast amputations are carried out for pathologic conditions other than carcinoma of the breast.

The percentage of patients who receive roentgenotherapy for carcinoma of the breast, while in the hospital, has noticeably decreased during the past two years. Approximately 45 per cent of the cases of carcinoma of the breast who leave the hospital without receiving roentgenotherapy return to the therapy department later.

Preoperative roentgenotherapy for carcinoma of the breast has become less popular during the past few years.



GRAPH V



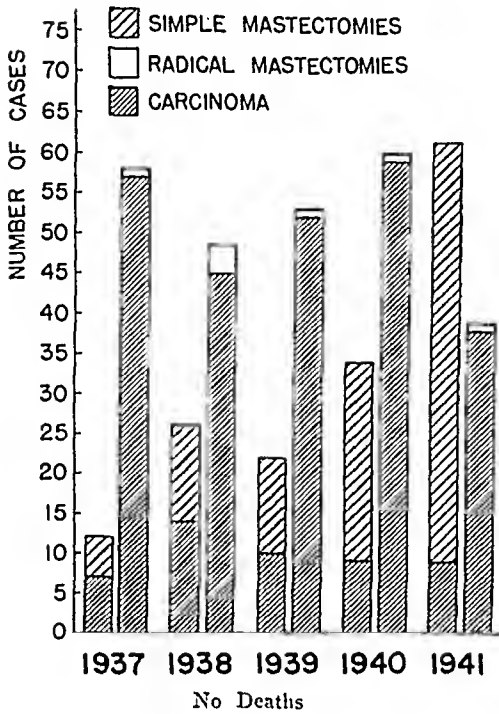
GRAPH VI

AMPUTATIONS

The total number of major amputations has always been small, and is decreasing. There were 26 amputations in 1937, and only 13 cases in 1941 (Graph VIII).

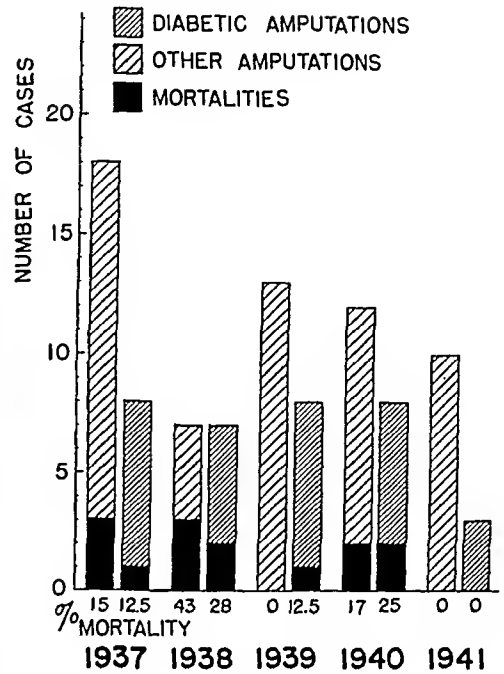
The mortality rate has been less in the presence of diabetes than for other diseases. The mortality rate for 13 major amputations during 1941

MASTECTOMY



GRAPH VII

AMPUTATION



GRAPH VIII

was zero. Only three were in diabetic patients (a marked decrease from previous years). The diagnoses of the other ten amputations in 1941 were: Emboli, thrombosis, senile gangrene, osteomyelitis, traumatic injury, thromboangiitis obliterans, arteriosclerotic gangrene, osteogenic sarcoma, fibrosarcoma, and osteochondroma.

ANESTHETIC AGENTS AND PROCEDURES

A review of the types of anesthetic agents and procedures employed reveals that 55 per cent of the patients received gas-ether anesthesia. Approximately 25 per cent were operated upon under spinal anesthesia, either alone or supplemented with inhalation anesthesia. There is a noticeable trend away from the use of nitrous-oxide alone as an anesthetic agent.

TABLE IX
ANESTHESIA (AGENTS AND PROCEDURES) FOR MAJOR AND MINOR OPERATIONS

	1937	1938	1939	1940	1941	Per Cent of Total for 1941
Gas-ether.....	4290	3813	3807	4054	4000	55.2%
Spinal.....	1740	1556	1311	1576	1834	25.4%
Ether (alone).....	275	271	313	324	394	5.4%
Nitrous oxide.....	461	392	279	116	131	1.8%
Cyclopropane.....	201	154	82	27	0	0.0%
Gas-evipal.....	1084	52	0	0	0	0.0%
Evipal (alone).....	6	46	11	10	0	0.0%
Avertin.....	4	7	1	3	0	0.0%
Sodium pentothal (alone).....	0	0	0	725	727	10.0%
Sodium pentothal plus ether.....	0	0	0	124	136	1.8%

Intravenous sodium pentothal anesthesia, introduced to Harper Hospital in 1940, has become very popular, especially for short gynecologic operations, fractures, amputations, and operations of necessity in debilitated individuals. In this last group it is often combined with local novocain infiltration. Cyclopropane, ethelyene, avertin and evipal were not administered during 1941.

BLOOD TRANSFUSIONS

In May, 1939, a blood bank was established under the supervision of Dr. Warren H. Cooksey. The bank effected three important changes in transfusion technic:

(1) Direct blood transfusions have steadily decreased, and, since the advent of the blood bank, have been almost completely eliminated.

(2) The number of direct transfusions has been greatly increased. There has been more than a 500 per cent increase in the total number of transfusions during this five-year period.

(3) Plasma transfusions, introduced in 1939, are increasing in popularity.

TABLE X
BLOOD TRANSFUSIONS

	1937	1938	1939	1940	1941
Total transfusions in the hospital.....	247	925	1441	1659	1451
Transfusions to surgical patients:					
(1) Direct.....	61	28	11	3	1
(2) Indirect.....	186	611	966	1084	993
(3) Plasma.....	0	0	15	34	74

SUMMARY

A review of the major surgical procedures at Harper Hospital for the past five years (1937-1941) shows the following trends and risks:

(1) The average mortality rate for major operations has ranged from two to three per cent during the past three years.

(2) The hospital autopsy rate is 35 per cent of the total deaths.

(3) Appendicectomy is the most common major operation, and represents one-third of all major surgical procedures. In 1941, the mortality rate was 0.3%. No deaths occurred from intra-abdominal complications. There were no deaths in 41 patients who had either generalized peritonitis or abscess.

(4) The mortality rate for 217 cholecystectomies during 1941 was 0.9%. Cholecystostomy is less frequent than previously; there were 30 such operations performed in 1941, with a 3.3% mortality rate.

(5) Gastrectomy is increasing but the mortality rate is still quite high, *i.e.*, 20 to 25%. The mortality rate for perforated peptic ulcer treated surgically is approximately 22%.

(6) The total number of radical resections of the colon and rectum has increased during the past few years. The operative mortality rate is 6%.

(7) The number of hysterectomies is increasing. The mortality rate for this operation was 0.7% in 1941. There were no deaths from total

hysterectomy in 1941, and 40% of all hysterectomies were total.

(8) Each year there are six or eight major abdominal wound disruptions, with a mortality rate of 30%.

(9) During 1941, 700 hernioplasties were performed. There were three deaths (mortality 0.47%) of which two were in cases of strangulated herniae.

(10) The mortality rate for thyroidectomy was 0.7% during 1941.

(11) There were no surgical deaths from radical mastectomy during this five-year period. The number of carcinomata of the breast treated surgically varies, but is not increasing. Simple mastectomy for benign lesions has increased.

(12) Major amputations are decreasing, especially in diabetic patients. There were no deaths in 13 major amputations performed in 1941.

(13) Intravenous sodium pentothal anesthesia, introduced to Harper Hospital in 1940, has become very popular. Cyclopropane, ethylene, avertin and evipal were not used during 1941.

(14) The introduction of the blood bank has resulted in (1) almost complete elimination of direct blood transfusions; (2) great increase in the indirect transfusion technic; and (3) an increasing administration of plasma transfusions.

REFERENCE

- ¹ Siddal, R. S., and Mack, H. C.: Subtotal Versus Total Hysterectomy. Surg., Gynec. & Obst., 60, 102, January, 1935.

BRIEF COMMUNICATIONS

INTRACRANIAL CALCIFICATION

REPORT OF AN EXCEPTIONALLY LARGE CALCIFIED TUMOR

RUDOLPH A. LIGHT, M.D.

NASHVILLE, TENN.

FROM THE NEUROSURGICAL SERVICE, DEPARTMENT OF SURGERY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

CALCIFICATION which is roentgenologically demonstrable occurs in many types of intracranial lesions and in some of them it occurs with great frequency, e.g., suprasellar cysts, 41 per cent,¹ oligodendrogliomas, 31 per cent,² or more.³

However, such calcification is usually demonstrable as small plaques or areas of flocculent-like increased density, and it is very rare to see a huge solid shadow such as that observed in the following case:

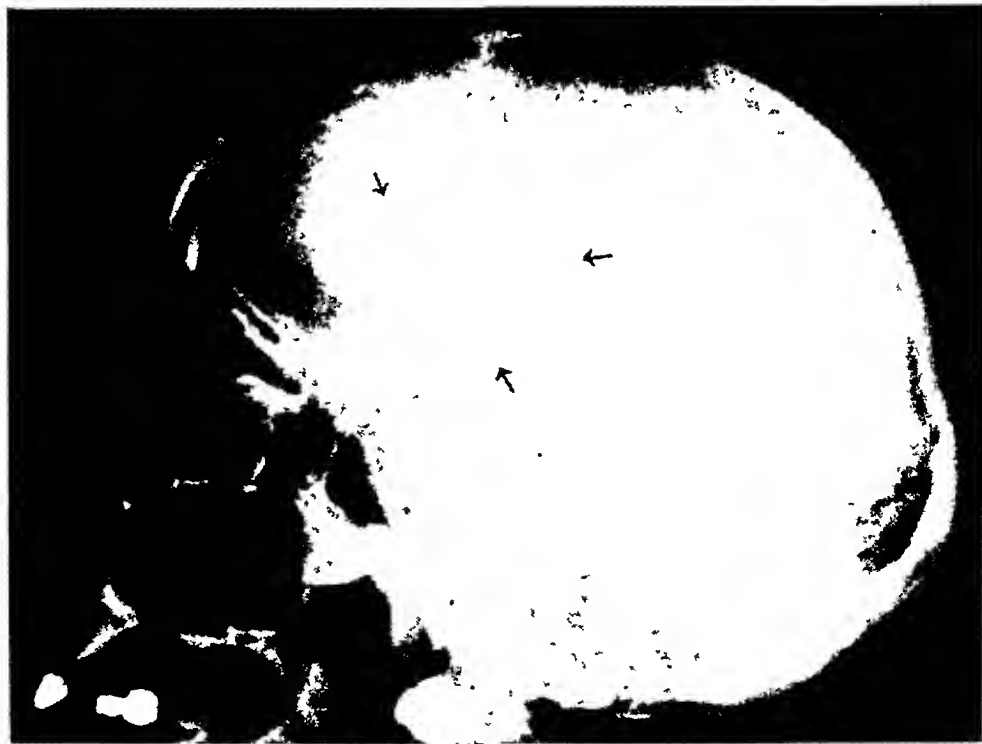


FIG. 1.—Lateral roentgenogram of the skull, showing the huge area of calcification in the frontal region.

Case Report.—V. U. Hosp., No. 108016: Referred by Dr. O. H. Clements, of Palmer, Tenn. D. F. C., white, male, age 40, was admitted June 25, 1940, with a history of having had generalized convulsive seizures for seven years. For four years his family had observed progressive mental disturbances. He became inattentive, grasped situations poorly, showed poor judgment, and had increasing difficulty in speaking correctly. He used words incorrectly and often repeated words or phrases without seeming to realize it.

During the year before admission, his vision had failed progressively to the point of almost complete blindness. For six months, he had vomited occasionally, but he had had headaches for only ten days. His family was aware of no localized weakness

or paresthesia. There was no history of injury or of relevant family disorders. He was right-handed.

On examination, he was well oriented, but memory was poor and cerebation slowed. There was no definite defect of speech. There was blindness in the left eye and only light perception in the right. The optic disks were choked. There was a central type of facial weakness on the right. No other disturbance of neurologic function was observed. There were no significant laboratory abnormalities.

Roentgenograms of the skull showed a huge, almost uniformly dense shadow, measuring 7 x 7 cm., in the left frontal region (Fig. 1). Its outline was jagged and irregular.

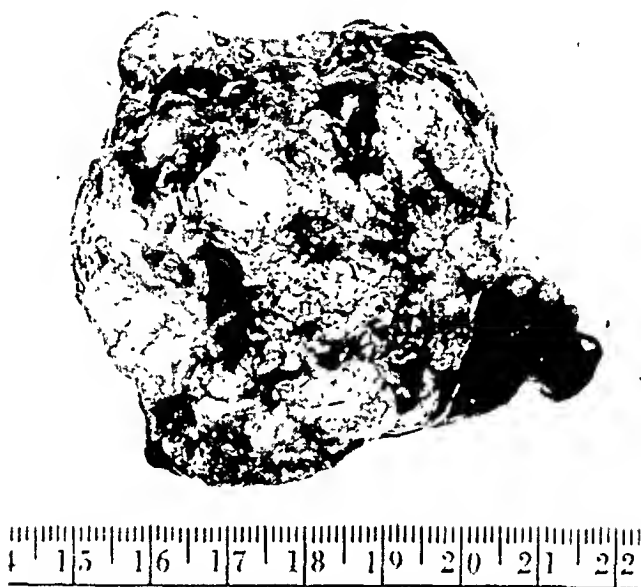


FIG. 2.—Photograph of the tumor.

Operation.—July 8, 1940: Dr. Cobb Pilcher. A considerable amount of soft, dark tumor tissue lay on the external surface of the calcified mass in the left frontal lobe, but, when the latter was gently enucleated, its bed was smooth and there was no sign of neoplastic tissue in its depths. The tumor was removed *en masse* (though no doubt there was infiltration in the cortical layers), and weighed 97 Gm. (Fig. 2).

The postoperative course was smooth for 48 hours, when the patient suddenly developed the unmistakable signs of postoperative hemorrhage. The wound was re-opened and a large hematoma evacuated from the tumor bed, but the patient survived the procedure only ten hours.

Histologic study showed the tumor to be an oligodendroglioma* (Fig. 3).

COMMENT

In 1916, Heuer and Dandy⁴ reported two cases in which there was extensive calcification in intracranial tumors. In one unoperated case, the shadow was irregular in outline and in density, and measured 4 x 5 centi-

* In the actively growing portion of the lesion the neoplastic cells were primitive, many mitoses were present and the tissue was quite vascular. Dr. Louise Eisenhardt of New Haven, who kindly examined sections of the tumor, classifies it as an oligodendroblastoma.

meters in its greatest dimensions. In the other, a shadow, 5 x 6 centimeters, was attached to the skull (which also showed an external palpable protrusion).† This shadow, too, was irregular and appeared somewhat flocculent in some areas.

O'Sullivan,⁵ in 1925, reported several fairly large intracranial calcifications, and Grantham and Smolik,⁶ have recently described a large area of

FIG. 3A

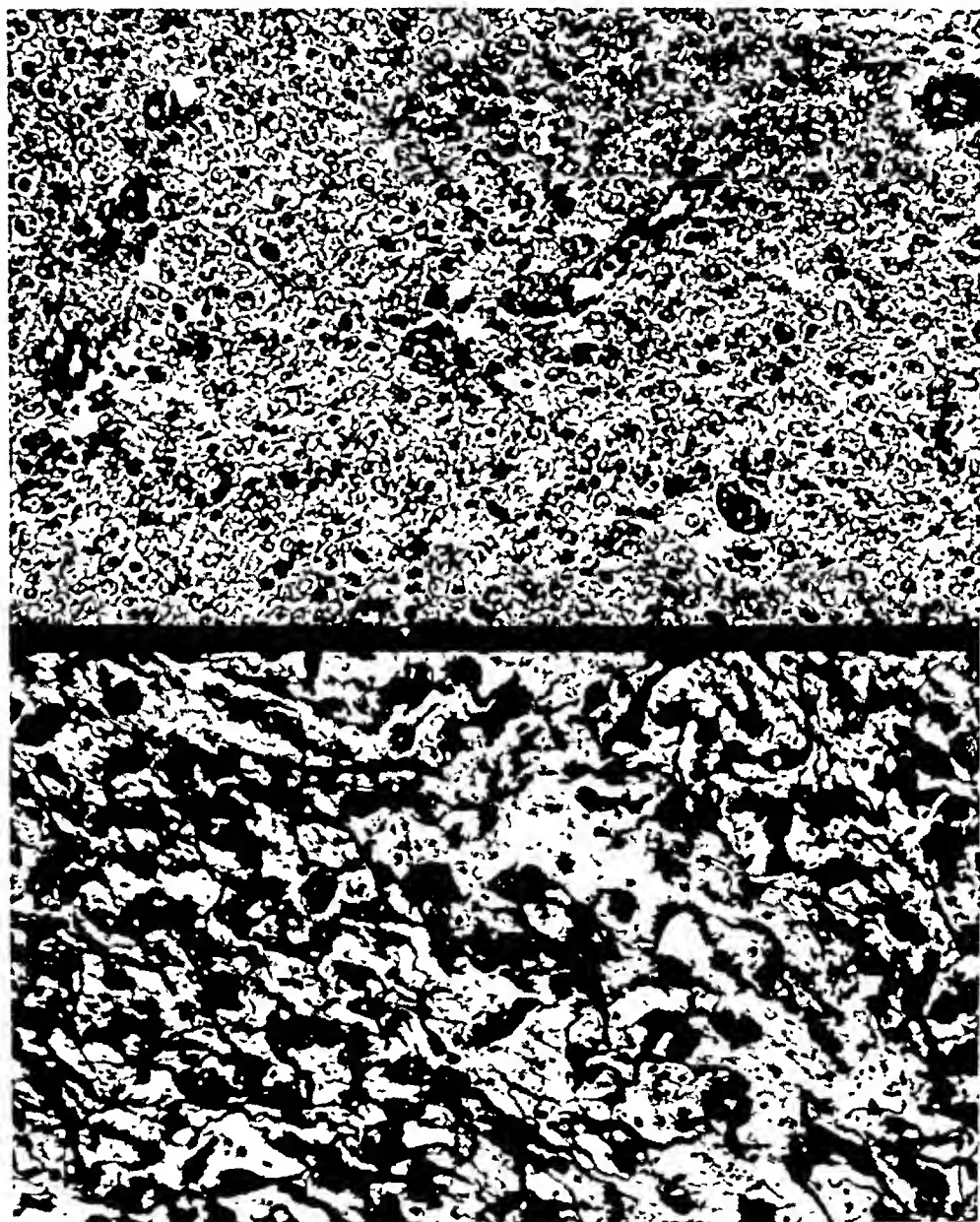


FIG. 3B

FIG. 3.—Photomicrographs of tumor. A. Note the poor staining qualities of the cytoplasm, giving the appearance of "halos" around the nuclei. Aniline blue-orange-G stain (reduced from a magnification of 250). B. The heavy protoplasmic processes of the tumor cells are uniformly impregnated. Penfield's silver method for oligodendroglia (reduced from a magnification of 250).

† This lesion was diagnosed osteosarcoma, but the author's description strongly suggests that it was a meningeal fibroblastoma.

calcification in an old intracerebral hematoma. Smaller calcifications of various types have been reported by many authors.

It is believed, however, that the tumor reported herein contained the largest area of calcification yet reported.

REFERENCES

- ¹ McKenzie, K. G., and Sosman, M. C.: The Roentgenological Diagnosis of Cranio-pharyngeal Pouch Tumors. *Am. Jour. Roentgenol. and Rad. Ther.*, **11**, 171, February, 1924.
- ² Bailey, P., and Bucy, P. C.: Oligodendrogliomas of the Brain. *Jour. Pathol. and Bacteriol.*, **32**, 735, October, 1929.
- ³ Van Dessel, A.: L'Incidence et le Processus de Calcification dans les Gliomes du Cerveau. *Archiv. Franco-Belges Chirurgie*, **28**, 845, October, 1925.
- ⁴ Heuer, G. J., and Dandy, W. E.: Roentgenography in the Localization of Brain Tumor: Based Upon A Series of 100 Consecutive Cases. *Bull. Johns Hopkins Hosp.*, **26**, 311, November, 1916.
- ⁵ O'Sullivan, J.: Some Rarer Intracranial Calcifications and Ossifications. *Brit. Jour. Radiol.*, **30**, 295, August, 1925.
- ⁶ Grantham, E. G., and Smolik, E. A.: Calcified Intracerebral Hematoma. *ANNALS OF SURGERY*, **115**, 465, March, 1942.

A NEW AUTOMATIC TWO-WAY VALVE

SIDNEY HIRSCH, M.D.

CEDARHURST, N. Y.

IN FEBRUARY, 1935, the author¹ described a simple automatic two-way valve to facilitate transfusions² and other therapeutic procedures, such as infusions, aspirations, phlebotomy, irrigations, *etc.* Since that time the unit has found considerable acceptance because of its proven value. In December, 1936, its successful use was recorded³ in over 125 citrate transfusions on the Pediatric Service of the Mount Sinai Hospital.

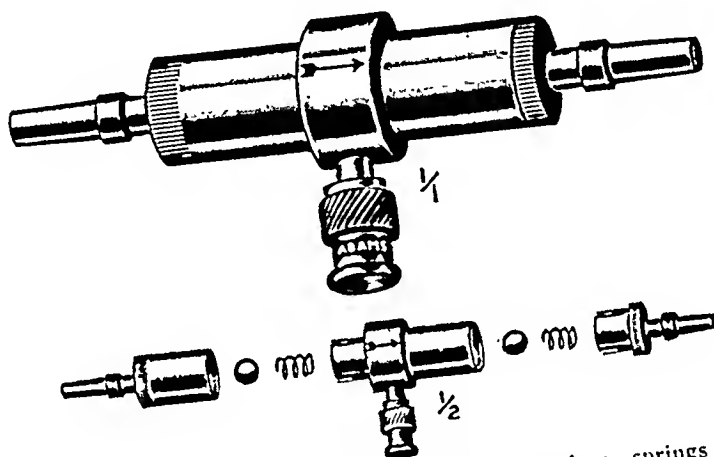


FIG. 1.—Unit taken apart showing ball valves, springs and direction of flow.

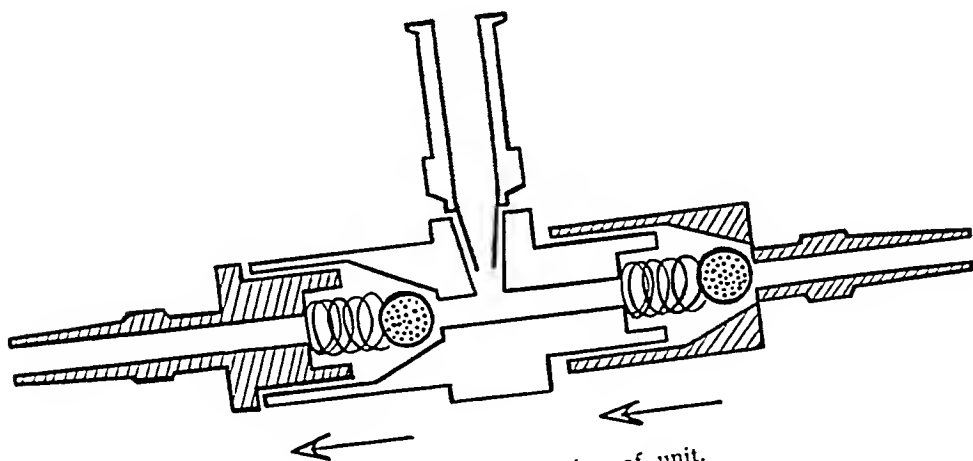


FIG. 2.—Diagrammatic view of unit.

Because of the war it has been very difficult to obtain the stainless steel from which the unit was made. To overcome this difficulty and to utilize more easily obtained and less essential metal, it has been found desirable to modify the unit somewhat. This modification permits the use of brass



FIG 3 —Complete set up with citrated blood in beaker and needle in recipient's arm

that is chromium plated and further permits the use of simple ball valves. Tiny springs, although not necessary, are included in the unit to insure perfect valve closures. Figure 1 illustrates the new apparatus. Its working principles are the same (Fig. 2). The upstroke of the syringe automatically opens the inlet valve and closes the outlet valve, and, conversely, the downstroke closes the inlet valve and opens the outlet valve. Both inlet and outlet fittings are so ground that either rubber tubing or needles may be attached directly to them. Its complete set-up for use is illustrated in Figure 3.

The fittings are removed by taking hold of the small, round, knurled nuts and pulling them out. The valves are easily removable, leakproof and airtight, so that there is no reflux. Any size Luer or record syringe with its adapter may be used with the apparatus.

REFERENCES

- ¹ Hirsch, S : Improved Blood Transfusion Apparatus ANNALS OF SURGERY, 101, 813, February, 1935.
- ² Hirsch, S.: Simple Glass Blood Transfusion Apparatus ANNALS OF SURGERY, 99, 553, March, 1934.
- ³ Hirsch, S.: Simplified Technique for Blood Transfusion in Infants Archives of Pediatrics, 51, No 4, 264-265, April, 1934.

FIRST-STAGE THORACOPLASTY

COMPLETE EXCISION OF THE FIRST THREE RIBS THROUGH SHORT ANTERIOR
AND POSTERIOR INCISIONS AT THE SAME OPERATION

EMILE HOLMAN, M.D.

SAN FRANCISCO, CALIF.

FROM THE STANFORD UNIVERSITY, SCHOOL OF MEDICINE, SAN FRANCISCO, CALIF.

INCREASED EXPERIENCE with operative procedures for collapse therapy in pulmonary tuberculosis indicate that long paravertebral incisions, passing around the angle of the scapula, with division of large masses of muscle, and vigorous anterior displacement of the scapula, are unnecessarily traumatizing and occasionally productive of shock through tissue injury and loss of blood. As an alternative procedure, particularly in men, and occasionally in women who are not adverse to a small scar visible to themselves, the following operative plan is submitted for employment in suitable cases:

Operative Procedure.—Under cyclopropane anesthesia, the patient is placed on the operating table lying on the unaffected side, and is so draped as to provide access to both the anterior and the posterior chest wall. This is made possible by covering the hand and arm with sterile stockinette, thereby including the whole arm and shoulder in the sterile field. Following complete draping, the patient is turned almost flat on his back for the performance of the first half of the operation. A short incision (Fig. 1a) is made parallel and three centimeters lateral to the sternal border running downward from the clavicle for about ten centimeters, passing through the pectoralis major muscle at right angles to its fibers. The second rib is mobilized first, and about 12 centimeters, including the entire costal cartilage, removed. The first rib is then isolated and about six centimeters removed together with most of its costal cartilage. The third rib is isolated last and about 10 to 12 centimeters removed, and if paradoxical respiration is not too pronounced, the costal cartilage is also removed. A more limited excision of the third rib anteriorly is indicated if paradoxical respiration is prominently present after resection of the first two ribs. As much of each rib as possible is freed of its periosteum lateralward, but only so much of the rib is removed as can easily be divided in the depth of the wound. Interrupted sutures of silk approximate the fascia of the pectoral muscle and the subcutaneous tissues, and a continuous suture of steel wire closes the skin. No drainage is provided.

Without changing drapes, the patient is rolled back on the unaffected side, the arm hanging forward in front of the chest. A short high incision (P in Figure 1) is made half-way between the spinous processes and the border of the scapula, passing through trapezius, rhomboid and serratus posterior muscles. The third rib is identified by palpation from above, and iso-

lated from transverse process to its free anterior end. The transverse process is also isolated, and removed together with the rib. Similarly, the posterior halves of the second and first ribs are isolated and removed together with their transverse processes.

To permit continuing and progressive compression as healing by fibrosis proceeds, regeneration of the excised ribs is inhibited over a short segment

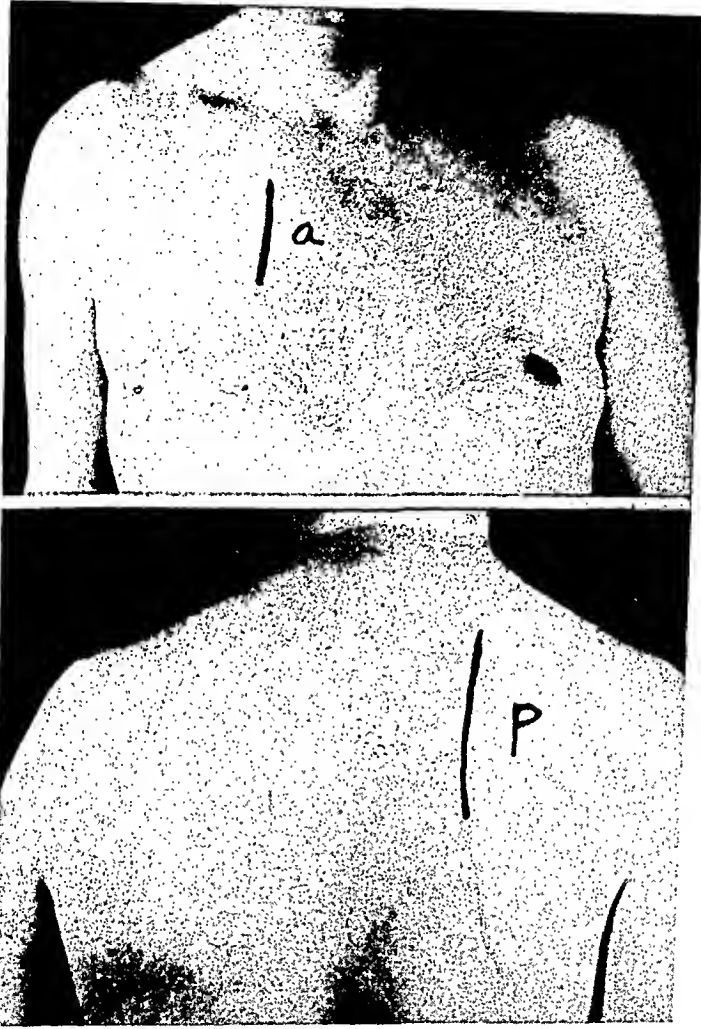


FIG. 1.—This patient was operated upon December 8, 1940, through two small anterior (a) and posterior (P) incisions for the complete removal of the first three ribs at the same operation. The posterior incision (P) was prolonged downward three weeks later for the removal of the posterior halves of the 4th, 5th, and 6th ribs, and partial removal of the lower third of the scapula, thus effecting closure of a large apical abscess.

by cauterizing, with the actual cautery or with the Bovey coagulating unit, the periosteum of the ribs for about three centimeters lateral to the site of the transverse process. The wound is closed by approximating the fascia of the trapezius muscle with interrupted silk sutures, and the skin is closed with continuous steel wire. No drainage is provided.

Postoperative care emphasizes a change of position through 90 degrees every hour during the first 36 to 48 hours, accompanied by six to eight

FIRST-STAGE THORACOPLASTY

flexion and extension exercises of arms and legs with each change of position. At about half-hourly intervals, when awake, the patient is asked to breathe deeply six or eight times. In the presence of bronchial exudate this usually initiates coughing and the bringing up of accumulated mucus. These precautions are most important: First, in preventing atelectasis secondary to the accumulation of mucus and exudate in dependent bronchi; secondly, in preventing abdominal distension by the avoidance of "water traps" in the intestines; and thirdly, in maintaining an active peripheral circulation to prevent femoral and peripheral venous thromboses and pulmonary emboli. These measures are considered vital in the postoperative care of all patients, but particularly after thoracic and abdominal operations. After the first two days, the patient is encouraged to change his position frequently, *unassisted*, using his own muscles rather than those of the attendant or nurse. Three hundred cubic centimeters of salt solution is instilled into the rectum every four hours for six doses, the first two instillations containing 60 grains of sodium bromide. Pain is controlled by pantopon, gr. $\frac{1}{6}$, injected hypodermically every three hours, if necessary.

Postoperative rises in temperature and pulse are usually minimal. A very gratifying feature is a very pronounced lessening in postoperative pain, and, consequently, a much greater willingness to execute the changes of position and perform the exercises which are considered so vital in effecting an uncomplicated convalescence.

The second stage of the thoracoplasty is undertaken about two and one-half to three weeks later, when three or four ribs are partially resected posteriorly through a short incision overlapping the lower third of the previous incision and extending downward from it for about 10 to 12 centimeters.

At the second operation for high apical abscesses, only portions of the fourth, fifth, and sixth ribs are removed, but under these conditions the lower third of the scapula is also excised to permit the remaining scapula to fall into the rib defect, thus producing compression where it is most needed, and conserving as much healthy lung as possible. When seven or eight ribs are removed, partial excision of the scapula is not necessary, as the whole scapula then falls naturally into the rib defect.

It should be emphasized that thoracoplasties through short incisions are possible, with confidence, only after having familiarized oneself thoroughly with the problem of rib resection through the longer and more revealing paravertebral incision. Part of each of the above procedures is necessarily accomplished through the sense of touch, rather than through the sense of sight.

SUMMARY

The first-stage upper thoracoplasty for pulmonary compression is effected with lessened shock and with lessened loss of blood when performed through

two small incisions, instead of through the conventional long paravertebral incision. The first incision is made anteriorly, paralleling the sternal border, through which the medial halves of the first three ribs together with their costal cartilages may be removed; the second incision is made posteriorly, paralleling the vertebral border of the scapula in its upper half through which the remainder of the first three ribs together with their transverse processes are removed, both incisions being made at the same operation. The second-stage thoracoplasty may be performed two and one-half to three weeks later through a second short posterior incision.

REFERENCES

- ¹ Wangenstein, O. H.: Thoracoplasty for Tuberculosis and Chronic Empyema through Short Incisions. *Jour. Thor. Surg.*, 8, 60, 1938.
- ² Finochietto, R.: Thoracoplasty without Section of Muscles. *Jour. Thor. Surg.*, 9, 450, 1940.
- ³ Head, J. R.: Extrapleural Thoracoplasty: Further Experience with a Muscle-Splitting Operation. *Jour. Thor. Surg.*, 8, 55, 1938.
- ⁴ Wylie, R. H., *et al.*: Thoracoplasty through Short Lateral and Posterior Incisions. *Surgery*, 2, 68, July, 1942.
- ⁵ Holman, E.: Partial Resection of the Lower Scapula as an Aid in Compressing Apical Tuberculous Abscesses and in Conserving Vital Capacity. *Jour. Thor. Surg.*, 6, 496, June, 1937.

**OUR MEN NEED
★ BOOKS ★**



**SEND
ALL YOU CAN SPARE**

That book you've enjoyed —
pass it along to a man in uni-
form. Leave it at the nearest
collection center or public
library for the 1943 VICTORY
BOOK CAMPAIGN.

BOOK REVIEWS

SYNOPSIS OF TRAUMATIC INJURIES OF THE FACE AND JAWS. By Douglas B. Parker, M.D., D.D.S. C. V. Mosby Co., St. Louis, 1942.

IN this little handbook of surgery, with 229 illustrations, the author has given us a very handy working manual that ought to be in the "haversack" of every dental and medical officer in the armed forces. The text is put together in a very logical and readable manner, and is up-to-the-minute in every detail in the treatment of traumatic injuries of the face and jaws.

In this global war, where front lines are created overnight, and where wild islands and harren coasts are invaded, very few maxillofacial centers will be established anywhere near the front, where the dental surgeon and the surgeon can carry out very advance treatment in the case of the injuries of the face and jaws. This is a war of movement and the medical and dental officers will have to supplement each other and in many instances do each other's work, which will often be "first-aid" in character. This guide book will help the medical officer in bringing together the hard and soft tissues of the face and jaws into approximation and will give the dental officer quite a lot of information in arresting hemorrhage, shock, infection, methods of resuscitation, and the reduction and fixation of fractures of the bones of the jaws and face.

There is practically no dentistry at the front, and, more than ever, the dental officer is called upon to give first-aid treatment either in the Army or Navy. This book will answer many questions quickly for the medical and dental officer at the front who is up against something that he has never seen before and needs help in a hurry.

The chapter on anatomy is clear and explicit and quite adequate for a book of this size. The author deals in a very practical manner with the "early treatment of the injury at the scene of the accident," and his remarks should tend to eliminate a lot of confusion, and help the patient get what he most needs in a hurry, namely, intelligent and skillful first-aid treatment. The early treatment of these face and jaw injuries, not only will give us better postoperative results, but in some cases will save lives.

The later treatment of wounds and burns of the face presented, is up-to-date, scientific and sound in every way. His treatment of bony injuries and the stabilization of fractures is most excellent and should be of great help to the medical officer who has had very little experience, as a rule, in the care of fractures of the bones of the face and jaws. The description of intermaxillary wiring and the different types of intra- and extra-oral splinting is most thorough and adequate.

Local anesthesia is also well cared for and, again, this ought to be a great help to the medical officer who is not so familiar with producing anesthesia of the face and jaws. Dr. Parker has been very successful in getting together excellent illustrations that go hand-in-hand with a clear, concise text, which makes this little guide a great help to the practitioner and will undoubtedly assist him in obtaining better end-results in this field of surgery.

The book being published at this time ought to help indirectly many of our boys now at the front who will need the best of care for wounds of the face and jaws.

HENRY SAGE DUNNING, M.D., D.D.S.



SULPHANILAMIDE AND RELATED COMPOUNDS IN GENERAL PRACTICE. Second Edition! pp. 374. Wesley W. Spink, M.D., F.A.C.P. Associate Professor of Medicine, University of Minnesota Medical School. The Yearbook Publishers, Inc., Chicago, 1942.

The subject of this book is one of tremendous importance and of widespread interest. The material is presented simply and clearly so that it enables the reader to get a comprehensive view of sulfanilamide therapy. The arrangement of the book is logical and it is indexed adequately for ready reference. It is not profusely illustrated but a number

of clinical charts are reproduced showing typical responses to chemotherapy in various conditions.

Suggested dosages of sulfanilamide for severe infections may seem a little high to some physicians as they do to the reviewer. While most physicians would agree that a moderate degree of cyanosis is not a contraindication to the continued administration of sulfanilamide, the severe degrees of cyanosis are sometimes a prelude to more serious toxic manifestations.

The author is to be congratulated especially on the chapters on "Historical Development" and "Toxic Manifestations." The book is concluded with a very valuable fifty-five page bibliography so arranged that the original sources dealing with particular phases of the subject of chemotherapy may be easily found.

J. E. RHODES, M.D.



TEXTBOOK ON FRACTURES. By Paul B. Magnuson, M.D. Fourth Edit., 1942. J. B. Lippincott Co., Philadelphia.

NO BETTER COMMENT can be made for this book than the fact that four editions have appeared in less than ten years, and the most recent one fully maintains the reputation that has been earned by the previous three.

It is more than timely in its appearance because its revision was not started until the certainty of our participation in World War II was established, making it possible for the author to anticipate the changes in treatment made necessary by the changing types of warfare.

The author has made an effort to express, in a concrete way, the accepted primary treatment and transportation of fractures as they occur in warfare, and, as he says, they represent the consensus of the Committee on Orthopedic Surgery of the National Research Council as constituted at the publication of this edition. Though the choice of methods in civil practice may be governed by circumstances and the judgment of the surgeon, in warfare; individualization to any great extent is not justifiable, and a more rigid standardization becomes necessary. However, such standardized treatments should be based upon a knowledge of the physiology and anatomy of the part involved, and a consideration of the fact that it is an injury to the body as a whole, and not just one part of it that requires the surgeon's care.

The text covers not only fractures of the long bones and joints, but includes the spine and hernia, in a way which should prove of great value to the military surgeon, who will rarely have had the advantage of a training in neurosurgery.

One is impressed by the lack of space devoted to open reduction of fractures of the long bones, and the use of fixation methods as employed by Boehler, Rodger Anderson and Stader, and it may be that sufficient time has not elapsed to properly evaluate these methods and determine their relative positions in the accepted methods of treatment of these injuries.

It would be difficult to find a more satisfactory piece of printer's work; the clear type, the paper, and the perfect illustrations not only attract but make the reading of the text more profitable than usual in a book of this size.

WALTER ESTELL LEE, M.D.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Pooks for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.

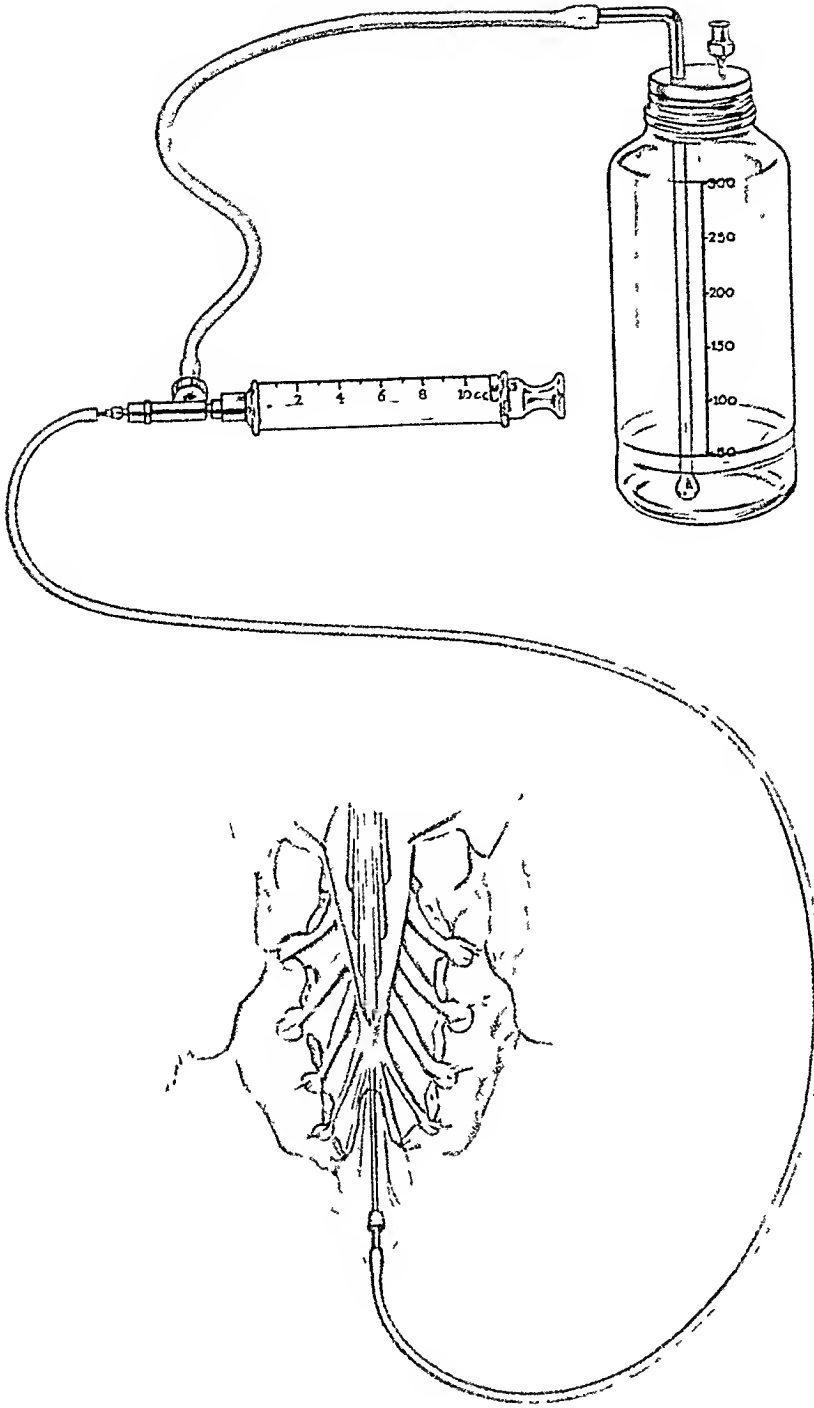


PLATE I—Assembly of needle, tubing, syringe and container for the solution of the anesthetic agent



CONTINUOUS CAUDAL ANALGESIA IN SURGERY*

JAMES L. SOUTHWORTH, M.D., WALDO B. EDWARDS, M.D.,

AND

ROBERT A. HINGSON, M.D.

STAPLETON, N. Y.

FROM THE UNITED STATES PUBLIC HEALTH SERVICE, MARINE HOSPITAL, STAPLETON, STATEN ISLAND, N. Y.

CONTINUOUS CAUDAL ANALGESIA, a method for prolonged caudal block, has been found useful in several types of surgical procedures. In some instances it has proved to be the anesthetic of choice. It is the purpose of this communication to discuss the application of the method, to note our recent experience with it, and to outline a technic for its administration.

There are several advantages which make continuous caudal analgesia worthy of consideration for use in general surgery. It is inherently a safe procedure and is comparatively easy to administer and control. The normal physiologic processes of the patient are little disturbed. It will find its field of greatest usefulness in operations about the lower extremities and the perineum, particularly in aged, debilitated, or recently shocked patients. It is also useful in inguinal and femoral hernioplasty. Further, it would seem that this method is adaptable for use in the treatment of casualties both in civilian and military practice where it would be desirable to have a safe, prolonged analgesia during the transportation and the physical and roentgenologic examinations of the injured. One anesthetist with several trained corpsmen or medical attendants could block a large number of patients at one time. It may be possible in some instances to block certain casualties on the field and transport them painlessly to a base for treatment, thus, perhaps reducing the instances of shock. On theoretic grounds it would seem that this method might be of value in the prevention of the delayed shock condition usually referred to as "crush" syndrome. Finally, limited experience in this hospital has shown promise that results similar to those obtained by Ochsner with lumbar sympathetic block in the treatment of thrombophlebitis and embolism of the lower extremities may be obtained with this procedure.

This method has been employed by us, and our associates, in more than

* Published with permission of the Surgeon General of the United States Public Health Service.

255 cases in general surgery, 150 of which were previously reported before the October, 1942 meeting of the American Society of Anesthetists. Table I lists the types and number of operations.

In three of these cases there were failures of the analgesia to reach the desired somatic level. In one instance, when given for inguinal hernioplasty, with a properly placed needle, the effect of the drug did not extend high enough to block the ilio-inguinal nerve in spite of shortened interval of injection and increased amounts of the drug. In the other two cases the failure was due to improper placing of the needle.

In inguinal hernioplasty the relaxation of the musculature is comparable to that of an expertly administered field block and often exceeds that of spinal. Traction on the cord and peritoneum in ligating the sac does not cause pain. An increased tendency to bleeding from the cut skin edges is noted. This tendency is not noted in the muscle layers should a vessel there be inadvertently cut.

In plastic operations about the vagina and perineum, it is an ideal analgesic. There is little interruption of the patient's usual routine of living. Meals are seldom missed either before or after the operation. The muscle relaxation is adequate. The presence of motor function in the extremities during and immediately after the operation tends to promote movement on the part of the patient, a condition thought to favor the prevention of thrombosis and embolism. The analgesia was satisfactory in three patients operated upon abdominally for lesions in the pelvis and for one undergoing cesarean section.

TABLE I
TYPES AND NUMBER OF OPERATIONS

Types of Operations	No. of Operations
1. Inguinal and femoral hernioplasty.....	43
2. Plastic operations on the perineum.....	21
3. Cesarean section.....	1
4. Hemorrhoidectomy; plastic operations about the anus; and abdominal operations on pelvic organs.....	34
5. Open and closed reductions of fractures of the lower extremities.....	24
6. Orthopedic procedures on the lower extremities.....	18
7. Amputations of lower extremities.....	7
8. Prostatic resection and other urologic procedures.....	41
9. Phlebectomy and ligation and injection of varicose veins.....	35
10. Appendicectomy.....	2
11. Treatment of thrombophlebitis.....	29

Those who prefer spinal anesthesia, or who undertake prolonged and meticulous operations for hemorrhoids, will find this method satisfactory. The relaxation of the anal sphincter is marked. Our experience indicates that the analgesia obtained from an expertly administered continuous caudal block is just as satisfactory as the seven-needle technic of sacral caudal block.

In orthopedic procedures on the lower extremity the method has been found of value in the recently shocked or elderly patient.

In urologic operations the advantages of complete lower analgesia without the dangers inherent in spinal anesthesia are present.

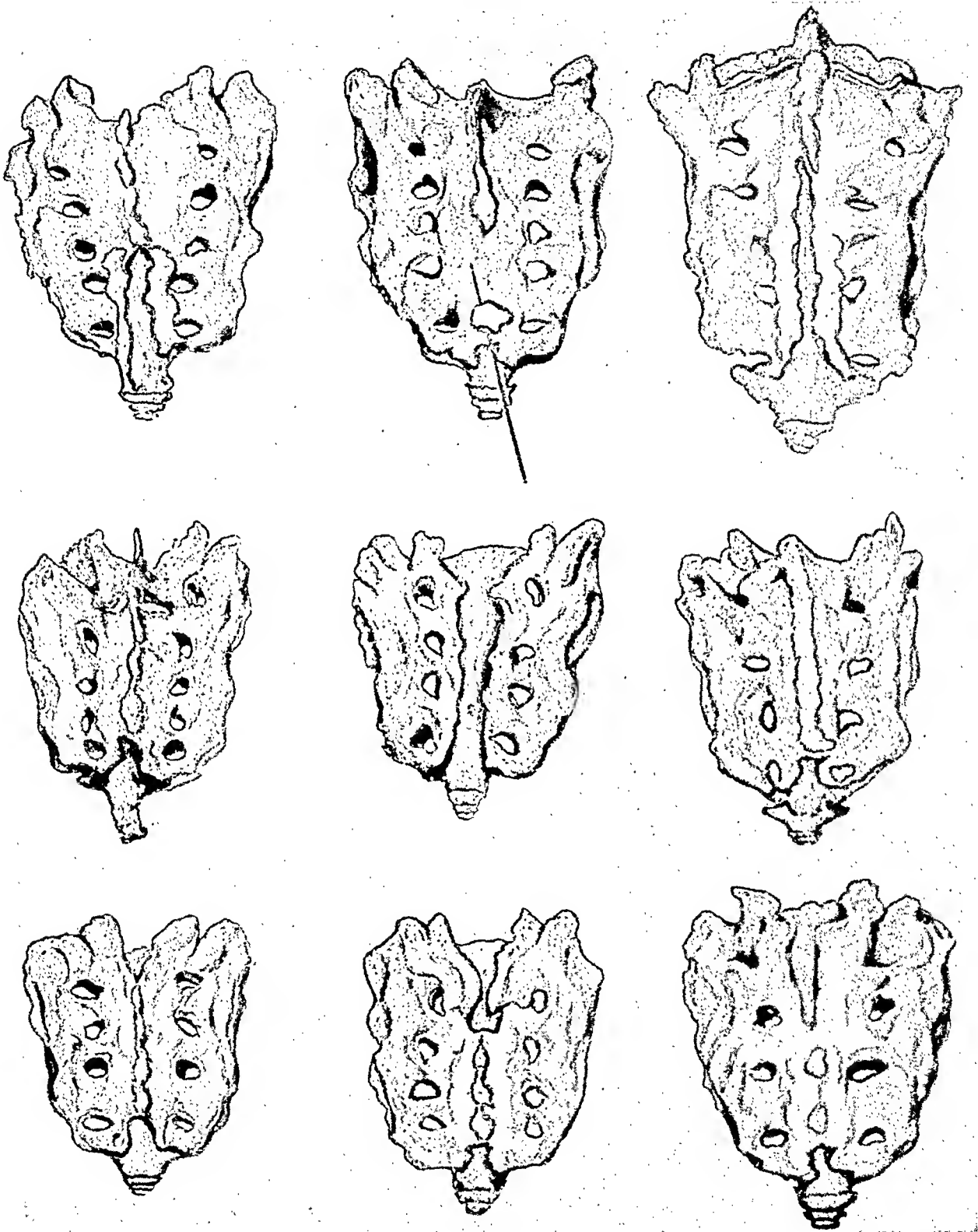


FIG. 1.—Common anomalies of the sacrum collected in the museum of anatomy from the Jefferson Medical College, Philadelphia, Pa. (courtesy Dr. George P. Pitkin: "Conduction Anesthesia," in preparation).

In phlebectomy an attempt is made to keep the dosage of the drug low so that the motor nerves are not affected. It has been found that the patient can aid the surgeon in maintaining position of the extremities during the operation.

With the present technic, the method is not recommended for appendicectomy, although in the two cases in this series it proved satisfactory.

In the treatment of thrombophlebitis promising results have been obtained. We have previously treated about 50 patients with the method of Ochsner in which lumbar sympathetic block is employed. The results were encouraging. The results in the patients treated with prolonged caudal block by the continuous method have been equally encouraging. It is our practice to maintain the block for four to six hours followed by a four-hour rest with the needle still in place. A second period of block of four hours duration is then administered. The following technic of administration is recommended for use in general surgery.

TECHNIC OF ADMINISTRATION

The patient is placed in the prone position and the sacral hiatus is palpated. The more common formations and anomalies of the sacrum, as shown in Figure 1, should be kept in mind. It is often of value to palpate the tip of the coccyx with the left forefinger and at the same time locate the sacral hiatus with the left thumb by palpation of the sacral cornua which lie on either side of the hiatus. The forefinger is moved to replace the thumb. The forefinger then serves as a guide to the location of the hiatus.

A continuous caudal set is assembled as shown in Plate 1. Since the use of the set shown, there have been no accidents involving broken needles in 200 consecutive injections.

The agent recommended is metycaine one and one-half per cent solution in physiologic saline. With this solution a skin wheal is raised just inferior to the hiatus. A special malleable No. 19-gauge needle is then inserted through the wheal and into the caudal hiatus, piercing, as it enters the canal, the sacrococcygeal ligament of Cathelin.

Careful aspiration should then be performed. If cerebrospinal fluid is withdrawn, it is recommended that the procedure be abandoned. This may occur in anomalous low-lying dural sacs. If bleeding through the needle is encountered, the needle should be withdrawn one to two centimeters and reinserted. When the bleeding has ceased the operator may proceed with the injection.

With the palm of the left hand firmly placed on the sacrum, ten cubic centimeters of the one and one-half per cent metycaine solution are injected. When the needle lies dorsal to the sacrum an "injection tumor" can usually be palpated. If the needle is correctly placed, the patient will complain of some unusual sensation in the lower extremities. This may be a transient ache, pain, or "shooting sensation" in the thighs or popliteal areas.

After the needle is properly placed, an average of 50 cc. of solution is

injected, according to the size of the patient. The analgesia begins in the areas supplied by the coccygeal nerves and progresses to those supplied by the hemorrhoidal, perineal, pudendal, ilio-inguinal and iliohypogastric nerves. Topographically, the analgesia usually begins about the coccyx and spreads in a circular manner up over the sacrum posteriorly and anteriorly over the perineum to the anterior abdominal wall. The toes begin to become insensitive to pain and the analgesia rises up the lower extremities. In the average patient analgesia will become complete from the umbilicus downward after 20 to 30 minutes.

A valuable sign that the needle is properly placed and the analgesia is progressing satisfactorily is the flushing of the toes and feet, which occurs within 5 to 15 minutes after the initial injection. Cold, moist feet become pink, warm, and dry.

Supplementary injections are given as required to maintain the desired analgesia. Twenty cubic centimeters every 30 to 40 minutes usually suffice. With proper precautions, the administering syringe may be placed near the field and supplementary injections may be administered by the surgeon or his assistant.

The work of the early investigators with single injection caudal analgesia showed that the height can be varied more or less in proportion to the speed of the injection and the amount of the fluid injected. We have found that when amounts larger than those recommended are used, and injected with more than the usual speed, analgesia can be obtained to the clavicles in many instances.

During the first 30 to 40 minutes after injection, the patient will not have complete loss of position sense although there will be absence of pain sensation to the umbilicus after 30 minutes. Increasing the amount of drug and decreasing the time interval between injections will cause a seepage of the agent anteriorly until the motor fibers are blocked. Patients subjected to the action of the drug, by this method, longer than one and one-half hours will also frequently exhibit this latter phenomenon.

The time consumed in the administration and the prolonged period during which the analgesia is incomplete constitute its most serious disadvantages. Thirty to 40 minutes are required to assemble the set, making the injection, and allow the analgesia to become complete. However, a skilled anesthetist, experienced in the method, can often have a patient ready for operation involving the perineum, vagina, or rectum in ten minutes.

As has been described in previous papers,^{1, 2, 3, 4} the complications arising from the use of the method have not been of great consequence in our hands. An occasional patient may experience mild syncope following the initial injection. It is thought that this may occur from one of two causes: (1) Either a small amount of the drug may have been injected into a vein, of which there are many in the sacral canal; or (2) it may be caused by sudden pressure on the dura from the injection of a comparatively large amount of solution. In our experience, the phenomenon has been transient (10 to 20 seconds

duration) and no sequelae have attended its occurrence. One moderately severe infection occurred in our entire personal experience. There was a low grade cellulitis about the sacral hiatus but there was no evidence of nerve injury. No other patient showed the slightest infection.

Failures of the method to produce the desired analgesia are due, in most instances, to the needle's being out of the sacral canal. It is sometimes difficult for one not specially trained and experienced in block anesthesia to insert a malleable needle directly in the midline and into the sacral canal. There are several common sources of error: The needle may lie superficial to the sacrum; it may lie in the periosteum of the roof or floor of the canal; it may lie within a blood vessel or within the subarachnoid space; or the needle may bend and come to lie lateral to the sacrococcygeal junction.

If a vein has been pierced at the beginning of the injection, a small hematoma may form about certain nerve trunks, giving patchy areas of sensation. Other than the failure of the analgesia in these areas, this has not been attended with sequelae in our series.

CONCLUSIONS

A. Continuous caudal analgesia has been found to be a valuable procedure in the following types of cases:

1. Plastic operations about the rectum and perineum in the fields of proctology, urology, and gynecology.
2. Operations below the umbilicus in the aged and debilitated, in which other forms of anesthesia are contraindicated.
3. Surgical and orthopedic repair of traumatism of the lower extremities.
4. Thrombophlebitis of the lower extremities.
5. Femoral and inguinal hernioplasty.

B. Experience indicates that the method is one of easy administration, accurate control, and one that can be prolonged as long as necessary, with little fear of complications.

REFERENCES

- ¹ Hingson, Robert A., and Southworth, J. L.: Continuous Caudal Anesthesia. *Am. J. Surg.*, **58**, 92-96, 1942.
- ² Edwards, W. B., and Hingson, R. A.: Continuous Caudal Anesthesia in Obstetrics. *Am. J. Surg.*, **57**, 459-464, 1942.
- ³ Hingson, R. A., and Edwards, W. B.: Continuous Caudal Anesthesia During Labor and Delivery. *Anesthesia and Analgesia*, **21**, 301-311, 1942.
- ⁴ Hingson, R. A., and Edwards, W. B.: Continuous Caudal Analgesia in Obstetrics. *J. A. M. A.*, **121**, No. 4, 225-228, January 23, 1943.

EARLY MORTALITY OF BURNS AS INFLUENCED BY RAPID TANNING AND BY TRANSFUSIONS

ROBERT ELMAN, M.D.

St. Louis, Mo.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY MEDICAL SCHOOL, BARNES HOSPITAL AND ST. LOUIS CHILDREN'S AND CITY HOSPITALS, ST. LOUIS, MO.

THE PURPOSE of the present communication is to draw a few inferences from a statistical study of the early mortality on over 400 cases of severe burns, with special reference to the type of local therapy and to the use of blood and plasma transfusions. The results of this limited study apply only to the important problem of reducing the early mortality, a feature of the treatment of burns which often has been neglected in favor of factors which deal with the subsequent treatment of these injuries. No attempt will be made to review the extensive literature on burns in view of the excellent summary reported by Harkins.¹

SELECTION OF CASES

In order to study only the more serious burns, all admissions of minor burns were excluded, *i.e.*, patients who were discharged to the Outpatient Department within 24 hours. Moreover, only patients whose end-result was known were included, *i.e.*, patients discharged to other hospitals were omitted from consideration. During the seven years from 1935 to 1941, inclusive, 369 cases treated at the St. Louis City Hospital were analyzed. In addition, 59 cases treated at the St. Louis Children's and Barnes Hospitals were reviewed briefly. The cases were divided first into two groups, depending upon the method of local treatment, *i.e.*, those in which tannic acid was used, and those in which no tannic acid was used. The latter group included a variety of local treatments such as the application of saline packs and soaks, vaselined gauze, various ointments such as pyrobaln, *etc.* Only a few cases were treated with triple dye, and these were included under the nontannic procedure. Local and systemic sulfonamide therapy was employed in many cases treated during 1941, but no special study was made of this fact.

The method of tanning employed should be emphasized; rapid coagulation was produced in each instance following cleansing of the burned area. This rapid coagulation was achieved by the alternate application of ten per cent silver nitrate and ten per cent tannic acid. In no instance was tannic acid jelly or the slower method of tanning with tannic acid alone used.

CLINICAL FINDINGS

A study of the cases analyzed was concerned largely with the influence on early mortality of (1) local therapy; (2) plasma and blood transfusions; and (3) priority in which local and systemic therapy was applied.

Influence of Tanning.—In the City Hospital an equal number of cases were treated by tanning in contrast to those treated without tanning; although the mortality was lower in the latter group, the difference is too slight to be of significance (Table I).

TABLE I

	Total Cases	Fatal Cases	Mortality
Rapid tanning.....	180	37	20%
Nontannic therapy.....	197	32	17%
Total cases.....	368	69	19%

A question may be asked in regard to the manner in which these cases were selected for local therapy. While it was difficult to determine always on what basis this selection was made, one fact tended to make the division rather accurate, *i.e.*, patients were admitted alternately on one of two different Services, and for various periods of time the policy of tanning was employed in one unit, whereas it was not used in another unit.

However, if one breaks down the 368 cases into yearly totals, the number of cases treated with tannic and nontannic therapy were equally divided during the years 1939 and 1940, and during these two years there was a striking difference in the mortality between these two methods of therapy (Table II).

TABLE II

	Total Cases	Fatal Cases	Mortality
1939—Tannic.....	31	4	13%
Nontannic.....	38	10	26%
1940—Tannic.....	25	2	8%
Nontannic.....	30	5	17%

Of interest, also, is the fact that two fatal cases in the tannic group in 1940 occurred at four and six hours, and received no plasma. This undoubtedly was a mistake in the priority of treatment, the local having preceded systemic therapy—a serious error which is discussed below.

The cases treated at Barnes and St. Louis Children's Hospitals were also analyzed in regard to a possible correlation between mortality and the use of tannic acid *versus* the nontannic acid therapy. Here the difference was significant and was similar to the experience at the City Hospital just noted (Table III).

TABLE III

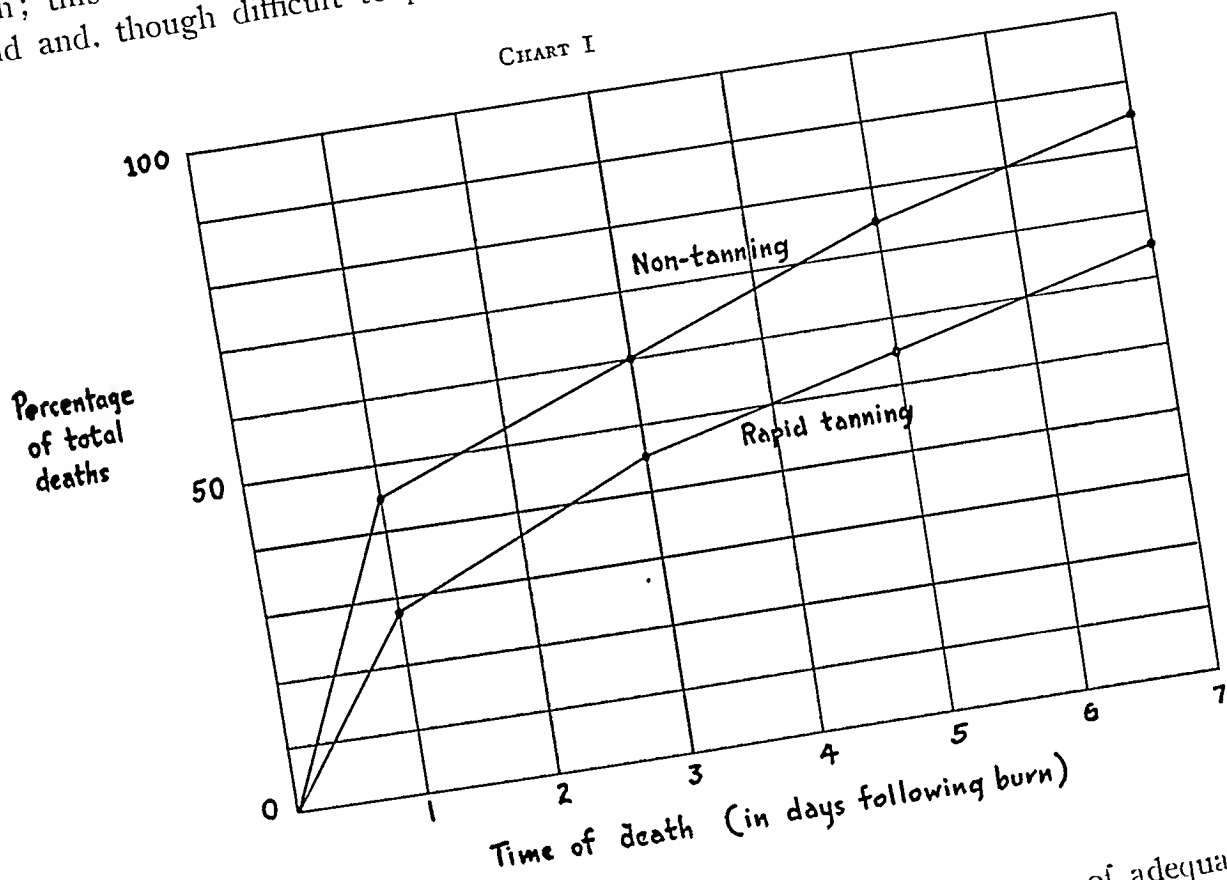
	Total Cases	Fatal Cases	Mortality
Tannic.....	15	1	7%
Nontannic.....	44	6	13%
Totals.....	59	7	11%

Of interest, too, was the fact that only one patient of the seven fatal cases received any blood or plasma.

The *time of death* in the St. Louis City Hospital cases was then analyzed, the fatal cases being again divided into two groups, one treated with and the other without tannic acid. The results were significant. It was apparent immediately that a smaller part of the patients treated with tannic acid died within the first few days than those treated without tannic acid. The difference has been plotted as a graph in Chart I, and is really self-

EARLY MORTALITY OF BURNS

explanatory. An obvious explanation of this difference is the effect of rapid coagulation in minimizing plasma loss. This inference is strengthened by the fact that, in more recent years, when large volumes of plasma were available, early deaths have diminished remarkably whether tannic acid was used or not. A second possible explanation is that the toxic absorption in cases burned, so as to produce wet, necrotic skin, was minimized by coagulation; this factor was the original basis upon which Davidson used tannic acid and, though difficult to prove, has, likewise, never been disproved.



Influence of Plasma and Blood Transfusions.—That the use of adequate amounts of plasma has reduced mortality in severe burns was apparent from simple inspection of the mortality figures from year to year. The mortality at the St. Louis City Hospital was 25 per cent in the year 1936, and has dropped steadily to a level of 11 per cent in the year 1941. Mortality figures are, of course, notoriously inaccurate because of the great influence of the severity of the burn. Nevertheless, such a difference in mortality in six years during which the only consistent change in therapy was the increased use of plasma seems a definite indication of this influence. This change, involving the increased use of plasma, concerns three details which may be mentioned at this point: (a) The gradual displacement of the use of whole blood by plasma. (b) The increased amount used in severe cases, i.e., as much as 5,000 cc. (c) The promptness with which plasma was used, made possible by the establishment of a plasma bank.

The influence of transfusions was even more strikingly evident when the fatalities at the St. Louis City Hospital were divided into two groups, *i.e.*, those treated with and those treated without plasma or blood. This analysis is listed in Table IV.

TABLE IV

Patients given no blood or plasma.....	25	
Death occurred within 24 hours.....	15	(60%)
Death occurred between 1 and 7 days.....	3	
Death occurred between 11 and 30 days.....	7	
Patients given varying amounts of blood or plasma.....	44	
Death occurred within 24 hours.....	6	(13%)
(of these, 3 received but 500 c.c. of whole blood, 1 received 1000 c.c. whole blood, and 2 each received 2000 c.c. of plasma)		
Death occurred between 1 and 7 days.....	21	
Death occurred between 8 and 90 days.....	17	

Note that, of the 25 fatal cases not receiving blood or plasma, 15, or 60 per cent, died within 24 hours, whereas only 6, or 13 per cent, of the 50 receiving this treatment died within 24 hours. Moreover, of the six cases in the latter group, four should really be listed as not receiving this form of therapy, inasmuch as the amount given was totally inadequate. If this transfer is made, it will be seen that only four per cent of the fatal cases given blood or plasma died within 24 hours, in contrast to 65 per cent in those receiving no blood or plasma, or inadequate amounts thereof.

The Influence of Priority of Treatment.—In analyzing the fatal cases in the present group, seven patients were found to have died within seven hours after admission. Study of these cases shows that the local treatment, often carried out under general anesthesia, was performed first and without adequate attention to systemic therapy, *i.e.*, the injection of plasma or blood. The inference, therefore, seems justified that certainly in a few of these instances, a fatality may have been avoided or at least postponed, if the treatment of shock were carried out immediately, and the local therapy delayed until the general condition had improved.

COMMENT.—The data analyzed in this study adds further emphasis to the importance of minimizing or correcting plasma loss *early* and *adequately*, if one is to lower early mortality due to shock. While a prompt and adequate plasma transfusion alone is quite satisfactory, rapid coagulation undoubtedly reduces the amount of plasma which is needed so that if the plasma transfusion is inadequate, this factor may tip the balance in favor of recovery. However, this is not the only beneficial effect which rapid coagulation probably has in reducing early mortality.

No one has yet disproved the original contention of Davidson that tannic acid, by coagulating dead tissue from which toxic products may be absorbed, minimizes or prevents the deleterious effects thereof. This theory depends, of course, upon the actual existence of *moist, necrotic* skin. The present writer has repeatedly observed such areas of skin in severe burns and believes that toxic absorption may occur whenever such a lesion is present just as easily as it can from nonviable intestine, from a wet gangrene of the leg, or

EARLY MORTALITY OF BURNS

from any other moist, dead tissue in which autolysis occurs with or without the presence of infection.

The fact that absorption of tannic acid has been shown to produce evidence of toxic hepatitis would seem to offer a contradiction to the mechanism just described. This discrepancy, however, is more apparent than real. In the first place, it is hard to see how, during *rapid coagulation*, significant absorption could occur. During *slow coagulation* which follows the use of tannic acid jelly, or of solutions of tannic acid alone, such absorption might easily occur, as pointed out by McClure and Lam.² Significant is the fact that in four cases of toxic hepatitis reported by Wells, Humphrey and Coll³ the slow method of tanning was used. On the other hand, Rhoads, Lee and Wolff⁴ have described two cases (Cases 11 and 14) in which death occurred on the fifth day, the autopsy showing toxic hepatitis, but in which tannic acid was not used. The problem of toxemia in burns is far from clear, and obviously requires further study. Until definitely disproved, however, the original hypothesis of Davidson should be retained as a possible explanation of some of the early deaths in burns which still occur in spite of adequate control of shock with early and sufficient plasma transfusions.

SUMMARY

A statistical analysis was made of 78 fatal cases among 427 severe burns, with special reference to the probable influence of therapy on the early mortality. It seemed clear that the following three factors alone or in combination contributed to early mortality: (1) The use of noncoagulation methods of therapy. (2) Failure to use plasma transfusions at all, or in inadequate amounts. (3) Failure to precede local by systemic therapy.

The inference seems justified that the reduction of early mortality depends upon giving rigid priority to methods which minimize or correct plasma loss and which thus combat, early and rapidly, the systemic manifestations due to loss of plasma. The problem of toxemia as a cause of early deaths is discussed briefly.

REFERENCES

- ¹ Harkins, H. N.: The Treatment of Burns. C. C. Thomas, 1942.
- ² McClure, R. D., and Lam, C. R.: Military Surgical Manuals—V. Burns, Shock Wound Healing and Vascular Injuries. W. B. Saunders Co., 1943, page 30.
- ³ Wells, D. B., Humphrey, H. D., and Coll, J. J.: New Eng. Jour. of Med., 26, 629-635, April 16, 1942.
- ⁴ Rhoads, J. E., Wolff, W. A., and Lee, W. E.: ANNALS OF SURGERY, 113, 955-960, June, 1941.

GOITER INCISIONS

FRANK H. LAHEY, M.D.
BOSTON, MASS.

FROM THE DEPARTMENT OF SURGERY, THE LAHEY CLINIC, BOSTON, MASS.

A GOITER INCISION involves many more features than are at first apparent. The appearance of the operative scar, very properly and importantly, occupies the mind not only of nearly every patient, certainly every female patient, but also the mind of nearly every surgeon. However, this is by no means the only feature of importance in connection with a goiter incision. Since a goiter, particularly when associated with hyperthyroidism and intra-thoracic goiter, possesses a high degree of possible fatality, it is most important that the incision provide complete and adequate anatomic exposure so that the surgeon can perform the operation without being hampered unnecessarily by technical complications, and with control of the thyroid's vascular supply. The method of making the incision and elevating the

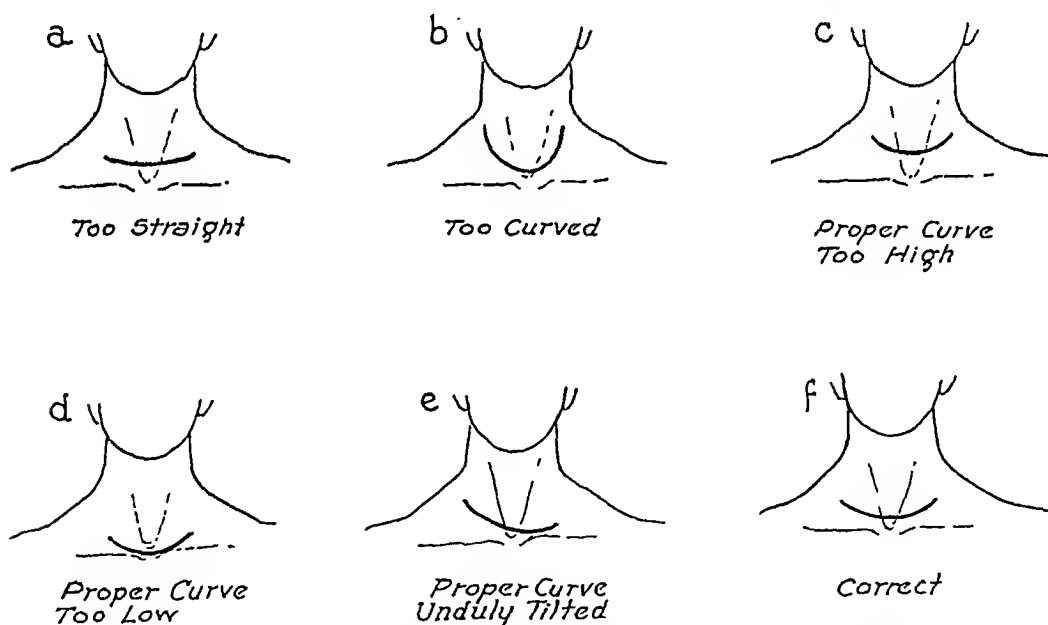


FIG. 1.—Showing various types of incisions employed for removing a goiter.

skin flap is also of great importance in what is often a serious procedure, since it influences the amount of bleeding and, therefore, also the length of time expended in controlling the bleeding and performing the operation.

Figure 1 a shows a goiter incision which is too straight and is unsightly because it cannot be concealed well by a necklace. A curved incision provides adequate exposure without particularly adding to the transverse length of the scar and so improves exposure.

Figure 1 b shows a goiter incision which is too much of the U- or horse-shoe-type. The same amount of exposure in the part of the wound high

GOITER INCISIONS

up beneath the skin flap can be accomplished with the symmetrical, slightly curved incision just above the junction of the neck with the chest without the unsightliness of this U-type of incision.

Figure 1 c shows a properly curved incision, but because it is placed too high it cannot be concealed satisfactorily by a necklace and is unsightly.

Figure 1 d shows a properly placed incision, but it is so low that it, likewise, cannot be concealed satisfactorily by a necklace.

FIG. 2.



FIG. 3.

FIG. 2.—The surgeon stands with his back to the patient's head in the proper position to make a well balanced, well curved goiter incision without having to swing his body.

FIG. 3.—When the surgeon faces the patient's head, it is difficult to keep the incision in balance, and the right side of the incision may be lower than the left. This is the position so often taken by those inexperienced with thyroid surgery, in order to visualize the neck.

Figure 1 e shows a properly placed and curved incision, but because it is improperly tilted and out of balance it is unsightly.

Figure 1 f shows a properly placed and curved incision of adequate length for exposure of all anatomic structures. Note that the curve corresponds with the level at which a necklace will hang, that is, just above the point where the neck joins the chest, which is the level at which the incision is least noticeable.

I have often been impressed when seeing a patient upon whom we have performed a subtotal thyroidectomy, the patient having had auricular fibrillation and cardiac decompensation and having been almost bedridden, that the first comment frequently is: "All my friends are so impressed with the beauty

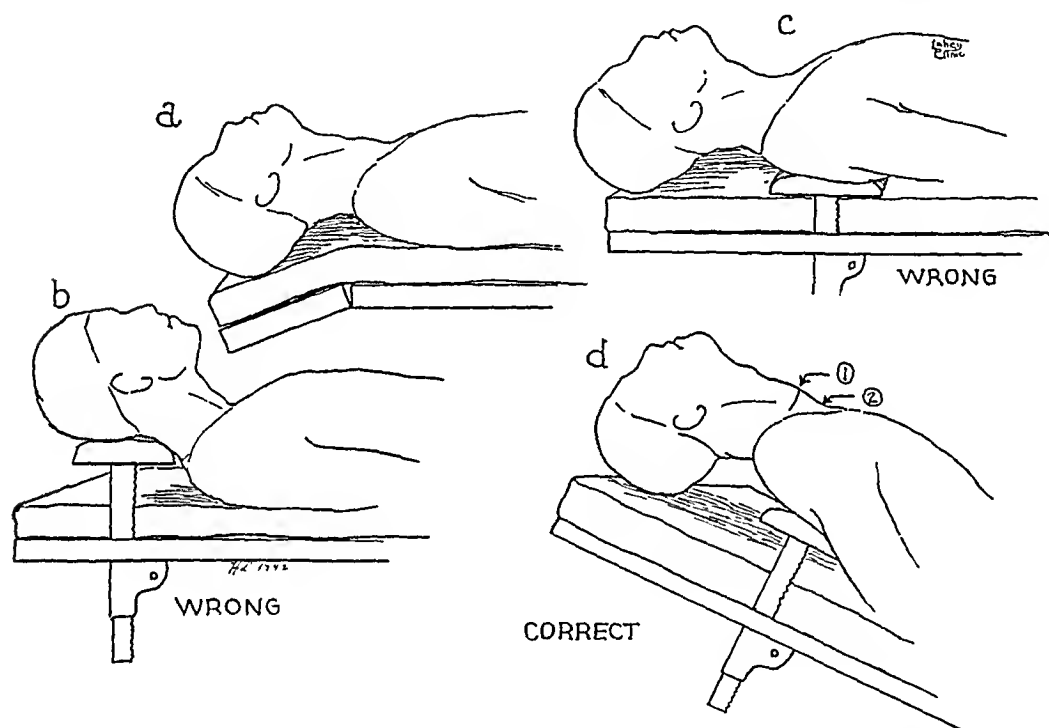


FIG. 4.—(a) The forward projection of the neck is inadequate when the head is dropped over the end of the table. (b) The goiter bar improperly placed beneath the neck, causing flexion of the neck on the wound. (c) The goiter bar properly placed well down beneath the shoulder blades. (d) The goiter bar properly placed beneath the shoulder blades. Forward projection of the thyroid can be obtained by elevating the chest. Arrow 1 shows where the incision must be made if it eventually is to be located at the point indicated by arrow 2, to which it will slip when the goiter bar is let down.

of this scar." In the meantime, normal rhythm has been restored, compensation retained, and all activities resumed, but elicitation of information concerning the physical improvement requires determined interrogation. This is not a critical observation, but indicates the necessity of satisfying the patient, and, after all, our obligation is to obtain the best possible scar in addition to the best possible exposure.

In the removal of 22,000 goiters we have learned many things about incisions. Not infrequently an assistant who comes to us inexperienced with goiter incisions is asked where he would make an incision. He often measures with the thickness of his fingers either one or two fingersbreadth

GOITER INCISIONS

above the notch of the sternum and arbitrarily settles that as the point of incision. For a number of years we have taught assistants that a well placed goiter incision should not depend on such an arbitrary rule. There are long and short necks, which vary between the tip of the chin and the hyoid, between the notch of the thyroid cartilage and the notch in the sternum. The only way a goiter incision can be well placed is by a free-hand marking of the neck and by determining with the eye, coordinated with the hand, the most artistic location and the proper curve of the scar.

A properly placed and gracefully curved goiter incision must be made with the knife poised rather loosely in the fingers, with the arm relaxed, and with a confident sweeping curve. It cannot be made slowly and cautiously since this involves tension, irregularities in the sweep of the curve, and a tendency toward distortion in balance.

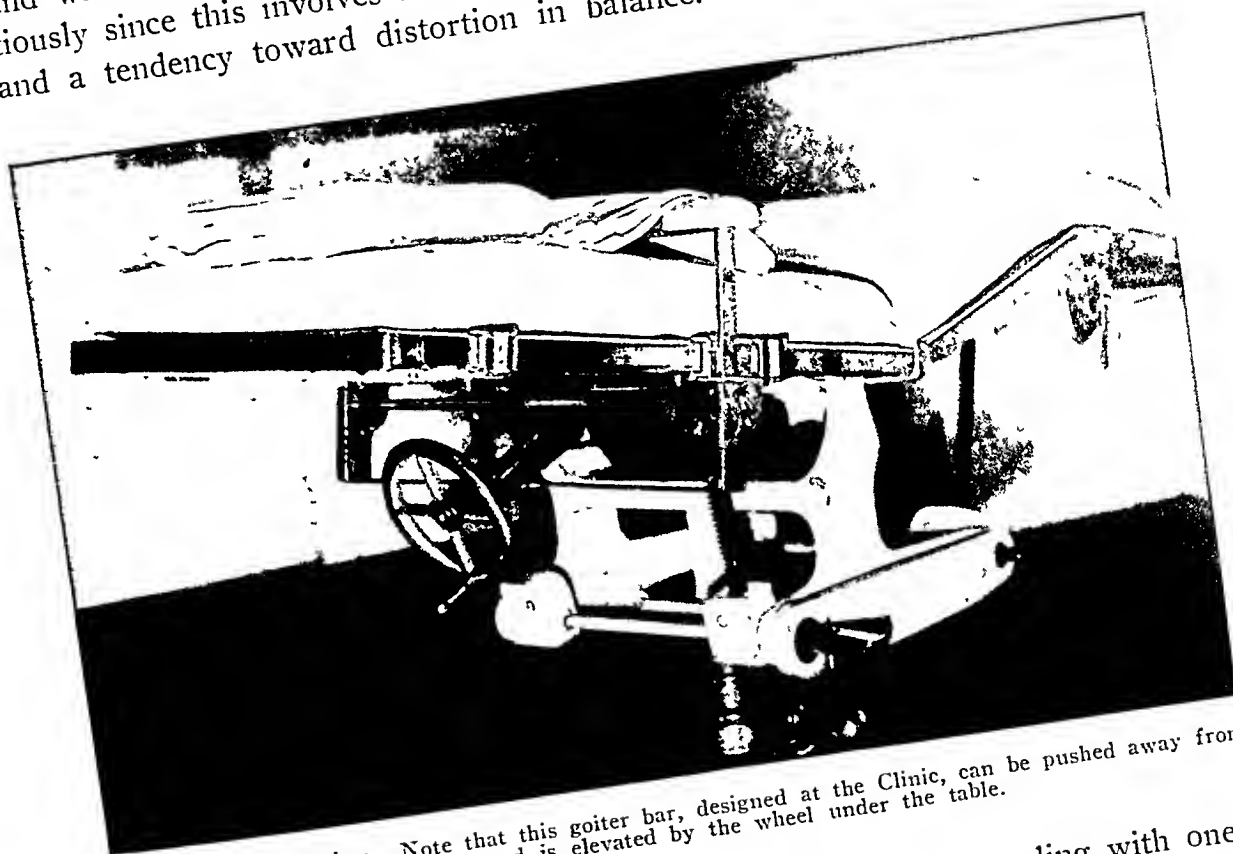


FIG. 5.—Goiter bar. Note that this goiter bar, designed at the Clinic, can be pushed away from or toward the head of the table, and is elevated by the wheel under the table.

There is a distinct advantage, in my experience, in standing with one's back to the patient's head in order to have a free arm and body turn, by means of which a curved incision can be completed as would be the case in free-hand drawing (Fig. 2). When the surgeon faces the patient's head and the knife is carried across the neck (Fig. 3), there is a tendency for the right side of the incision to be lower than the left. The two sides can be kept in balance only by compensatory rotation of the body or by twisting the wrist. Undoubtedly many surgeons can make a good incision while facing the patient's head, but it is easiest for me to keep the curve of the incision in proper balance if I stand with my back to the patient's head. Although this may seem like a small point, it does much to facilitate

a good incision not only for those surgeons who lack wide experience in thyroid surgery but also for those who have had extensive experience.

A forward projecting position of the neck in goiter operations is of the utmost importance not only in making a good incision but, also, in dealing technically with partial or complete removal of the thyroid gland. Attempts to obtain good exposure by permitting the head to drop over the end of the operating table or on a table, the upper end of which drops (Fig. 4 a), do not compare favorably with the results obtained with elevators properly placed beneath the shoulder blades (Fig. 4 c). Goiter bars, which permit

FIG. 6.

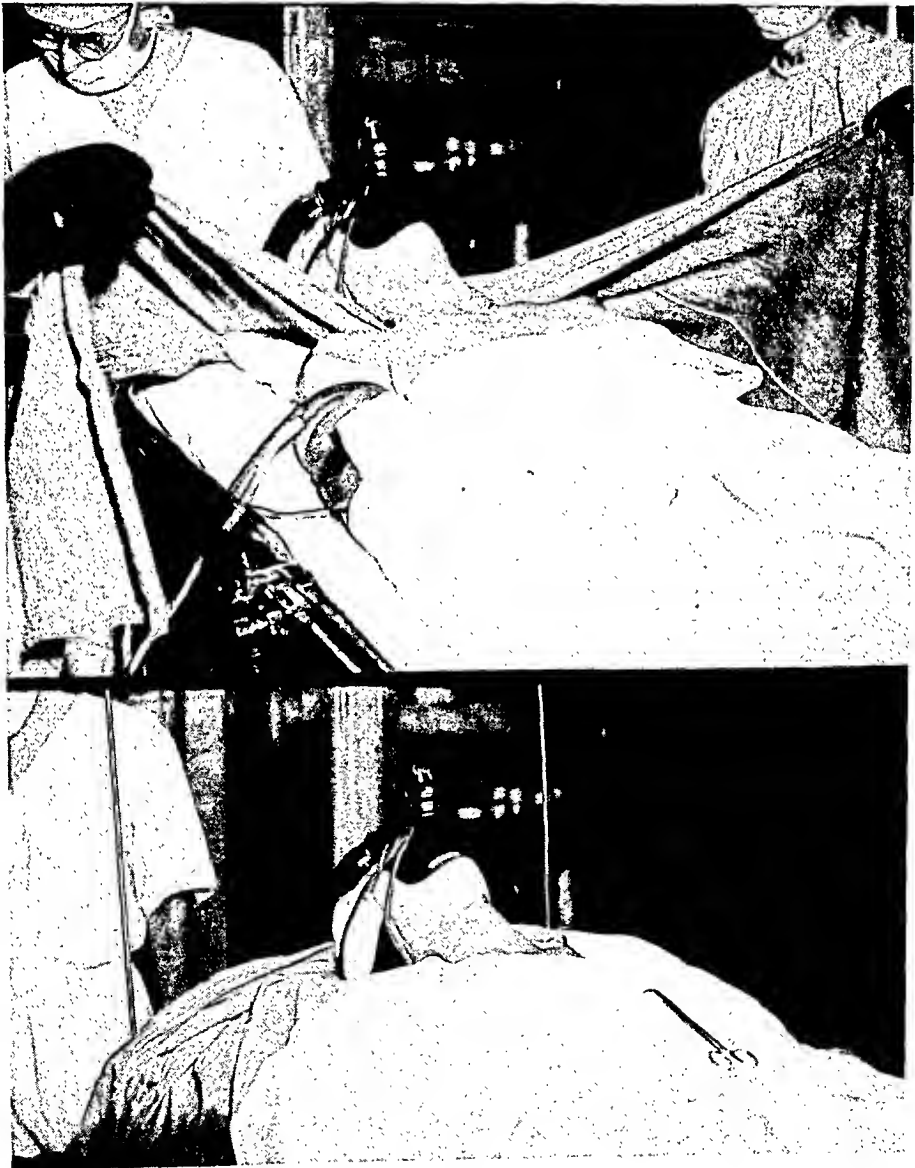


FIG. 7.

FIG. 6.—Draping for thyroid operation. The rubber tube connecting the anesthesia apparatus is removed, the head raised by the anesthetist, and a sterile sheet draped under the neck and head and carried down over the chest.

FIG. 7.—In the second step of draping, two towels forming a V are placed on the patient's chest and over the shoulders.

GOITER INCISIONS

elevation of the neck, have existed for a good many years; however, they are often misused. The goiter bar should not be placed beneath the neck (Fig. 4 b), since in this position it forces the head forward, the chin downward, and hinders rather than aids the exposure of the thyroid gland. If it is properly placed well beneath the shoulder blades (Fig. 4 c and d), it throws the chest up and so widens the distance between the chin and the sternal notch that it throws the neck forward, puts the skin on the stretch

FIG. 8.



FIG. 9.

FIG. 8.—In the third step of draping, a sheet is clamped across the patient's neck, the towel clip catching this sheet, the edge of the two towels which form a V, and the edge of the sheet which was placed beneath the head and neck. When this sheet is turned upward (Fig. 9), the operative field is exposed.

FIG. 9.—The sheet is draped over the anesthetist's frame. A sheet with a U cut-out is now placed over the patient's body and chest. With the U clamped to the sheet and a towel to the sheet over the anesthesia frame, the operative field is now completely draped. With strips of gauze tucked down in the angles beside the neck, an adequate amount of neck and chest is exposed and the anesthetist completely excluded.

and forces the thyroid into the wound when the prethyroid muscles are severed. I mention this method of exposure further to warn that as the neck is arched forward, one must be careful to make the incision a little higher than one wants the scar to be because when the goiter bar is let down, the incision will descend toward the sternal notch from one-fourth to one-half inch (Fig. 4 d, 1 and 2).

Another important factor in a goiter incision is the exposure of a sufficient area of skin over the chest and up over the neck as the wound is draped, permitting the establishment of good visual relations as to the proper level for the incision. I have frequently seen a goiter incision made through a very small aperture in the towels, giving little opportunity to relate the extent and location of the incision to the remainder of the

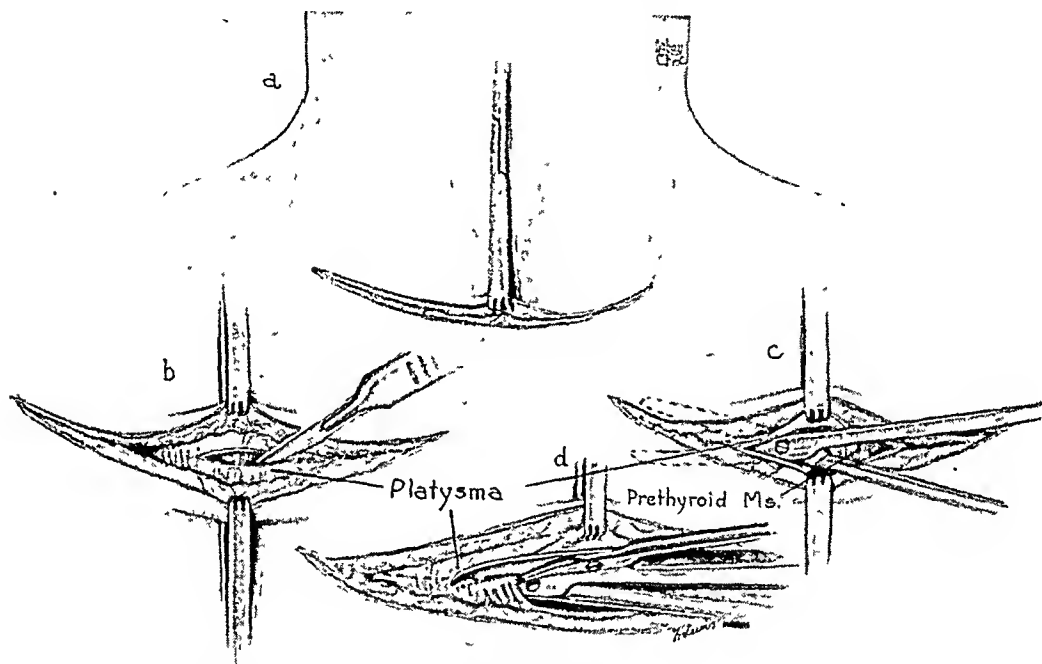


FIG. 10.—(a) Method of marking out the incision partly through the skin and not penetrating the entire thickness of the skin. (b) The incision is deepened until the platysma can be demonstrated and incised in the midline. (c) Metzenbaum scissors are inserted beneath the platysma to separate it from the prethyroid muscles. (d) The platysma separated from the underlying structures is now incised with scissors. This maintains intact the layer of adipose tissue between skin and platysma muscle.

neck and chest. In Figures 6, 7, 8 and 9 is shown the method utilized in this Clinic of draping thyroid patients. A good exposure of the neck is obtained, and the anesthetist is excluded completely from the operative field.

For many years we have taught that the first part of a goiter incision should extend only through the superficial one-half or two-thirds of the skin (Fig. 10 a); it can then be deepened in its central point (Fig. 10 b), through the skin, subcutaneous fat and platysma. As the platysma fibers are cut, platysma, subcutaneous fat and skin can be picked up above and below with double hooks. A pair of Metzenbaum scissors can then be introduced (Fig. 10 c) and opened beneath the platysma and in front of the prethyroid muscles so that the platysma is separated completely beneath both sides of the marked

GOITER INCISIONS

out skin incision. The central portion of the incision which already has been deepened can then be elevated, and the marked out skin with the subcutaneous fat and the elevated platysma can be cut with scissors in one layer on each side (Fig. 10 d). This retains the attachment of the platysma to the subcutaneous fat, and double hooks are so applied between the skin and platysma that the platysma envelope enclosing subcutaneous fat is kept intact (Fig. 10 c and d). This layer just beneath the platysma demonstrates the proper avascular line of cleavage between the platysma

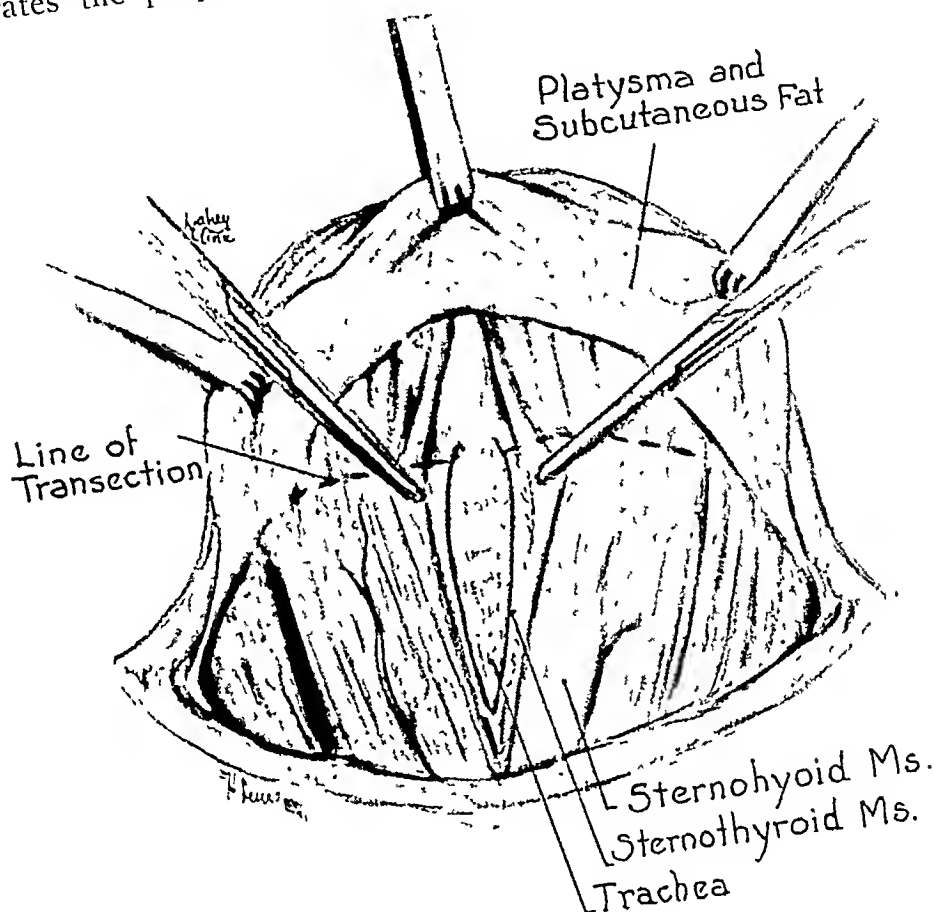


FIG. 11.—The method of folding the skin flap and moving the double hooks from the cut edges down to grasp the double fold of skin flap, thus facilitating its elevation to a high level. The level of transection of the prethyroid muscles is shown, as well as the second layer of muscles, the sternothyroid.

and prethyroid muscles. The flap, then consisting of skin, subcutaneous fat and platysma, can be delicately dissected up until it is well established, and by means of gauze pads can be wiped up with relative bloodlessness to any upper level of height which is desired. This is important because if the incision is carried up between the skin and platysma, the well vascularized subcutaneous fat bleeds considerably and requires considerable time and fussing for control. If the incision is unduly deepened beyond the platysma, the large, prominent veins adherent to the prethyroid muscles will be severed, control of the bleeding will consume considerable time, and the blood will interfere with the anatomic dissection of the skin flap upward.

I do not wish to give the impression that a good goiter incision cannot be obtained by elevating the skin flap in the subcutaneous fat plane between the skin and prethyroid muscles. From my experience, however, there are real disadvantages to the elevation of a skin flap in this plane: (1) Since dissection actually must be upward, it is more difficult and requires a greater amount of time to control the bleeding; and (2) greater postoperative edema occurs since traumatized fat reacts with swelling and edema in the skin

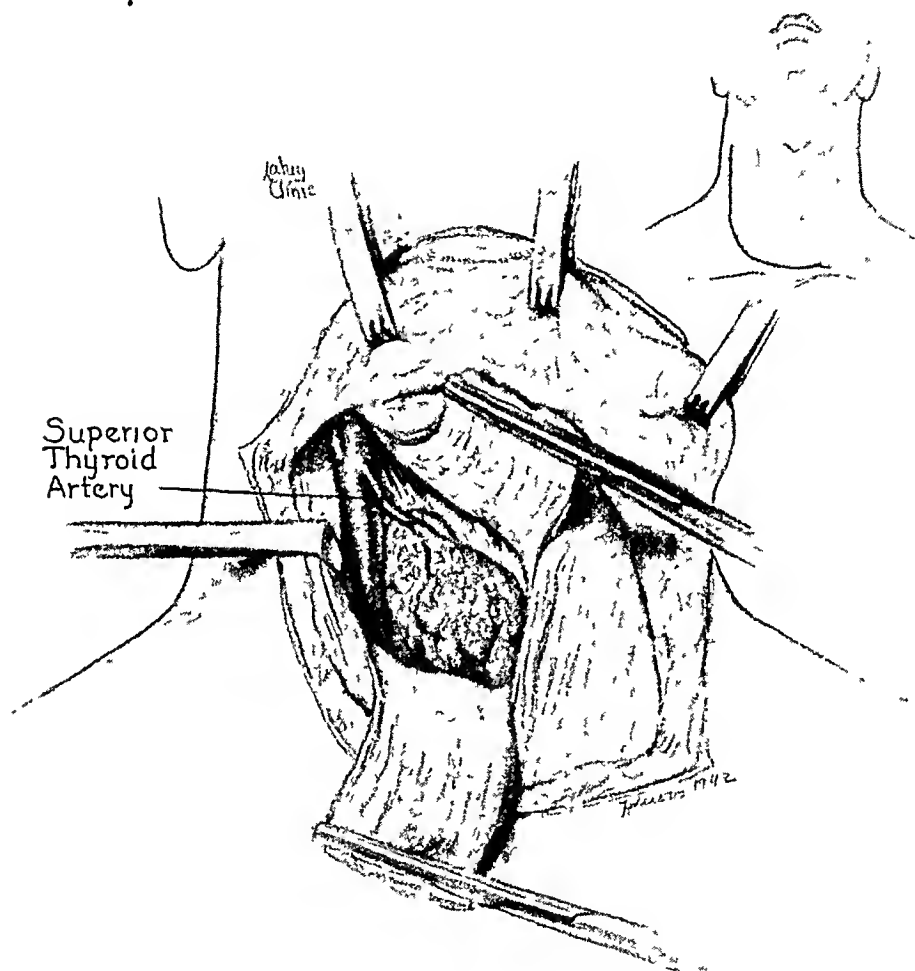


FIG 12—The insert shows the method of continuing the goiter incision upward on the side of the neck when serious secondary superior thyroid hemorrhage has occurred postoperatively. The large illustration shows the exposure of the first branch of the external carotid, the superior thyroid. This exposure facilitates prompt and complete control of superior thyroid artery hemorrhage.

flap much more than when the fat layer is retained untraumatized and when the flap is elevated in the plane as described, between platysma and prethyroid muscles. In addition, when the skin flap is elevated in the layer of subcutaneous fat between the skin and prethyroid muscles, dimple-producing, synechia-like scars develop postoperatively between the skin and subcutaneous fat. This does not leave the same freely movable skin flap that results when the subcutaneous fat layer between the skin and platysma remains undisturbed. In addition, the less trauma there is to

GOITER INCISIONS

the subcutaneous fat in the immediate vicinity of the wound the less reaction there is in the scar. I believe it is of real value, therefore, to grasp the platysma, once it has been demonstrated by the procedure above described (Fig. 10 c), with double hooks throughout the wound so that as the flap is lifted up and wiped up the platysma is not pulled away from the wound edge of the upper skin flap and a large amount of subcutaneous fat exposed.

We have found it unnecessary to undermine or to pull down the lower skin flap. Literally thousands of goiter incisions have been made in this Clinic without mobilizing the lower skin flap in any way and without impairing the appearance of the scar.

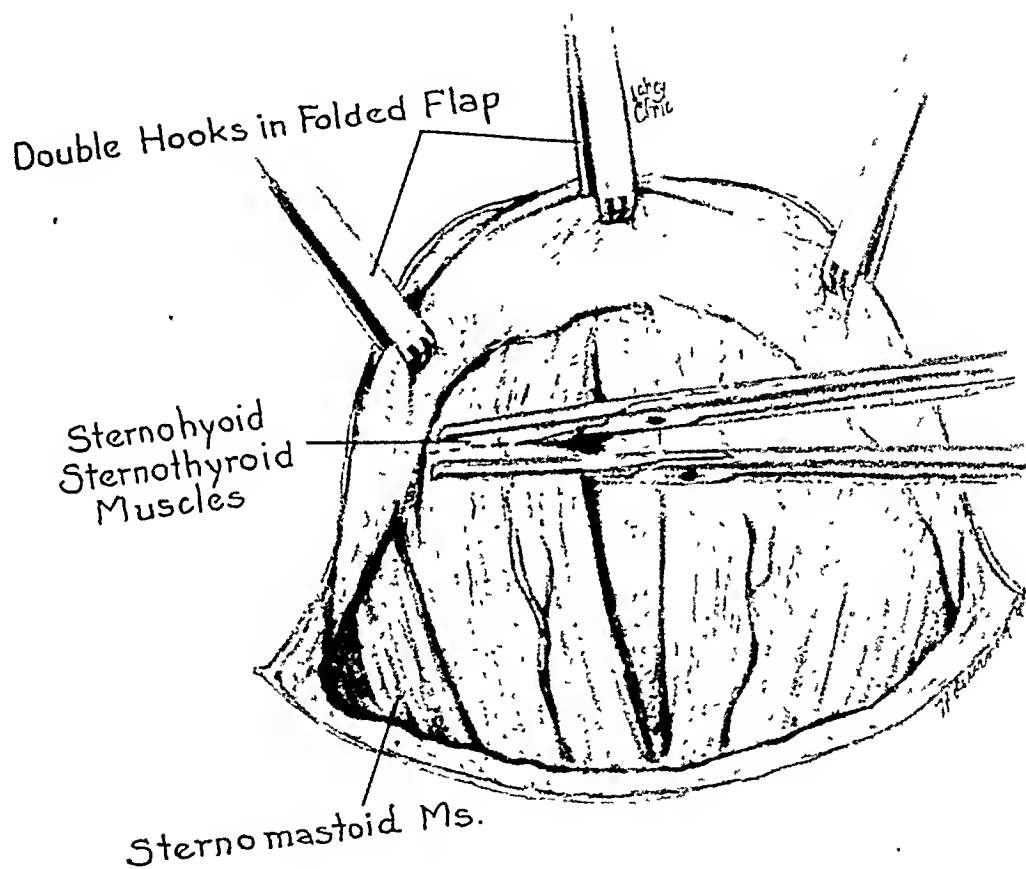


FIG. 13.—The method of grasping the double fold of upper skin flaps to facilitate its upward dissection well above the high level at which the prethyroid muscles are cut in order to avoid destroying their innervation and to stagger the muscle suture and skin suture at different levels (Fig. 15).

As the assistant soon learns, elevation of the skin flap up to the level of the notch of the thyroid cartilage is relatively simple since the fascial plane between the prethyroid muscles and the platysma is loose and well established up to this level. From here on it is not as well established and frequently requires sharp dissection. In order to obtain adequate exposure of the point where the superior thyroid artery enters the upper pole of the thyroid, all skin incisions should be elevated well above the level at which the upper pole of the thyroid can be palpated. This high elevation of the

skin flap often requires considerable determination on the part of the surgeon and willingness to face at times troublesome oozing from small vessels. In my opinion, no goiter incision is satisfactory unless the skin flap is elevated to such a level that at least an inch of the superior thyroid artery can be seen beyond the point at which it enters the apex of the thyroid gland. Figure 11 shows the method of grasping the folds of the upper skin

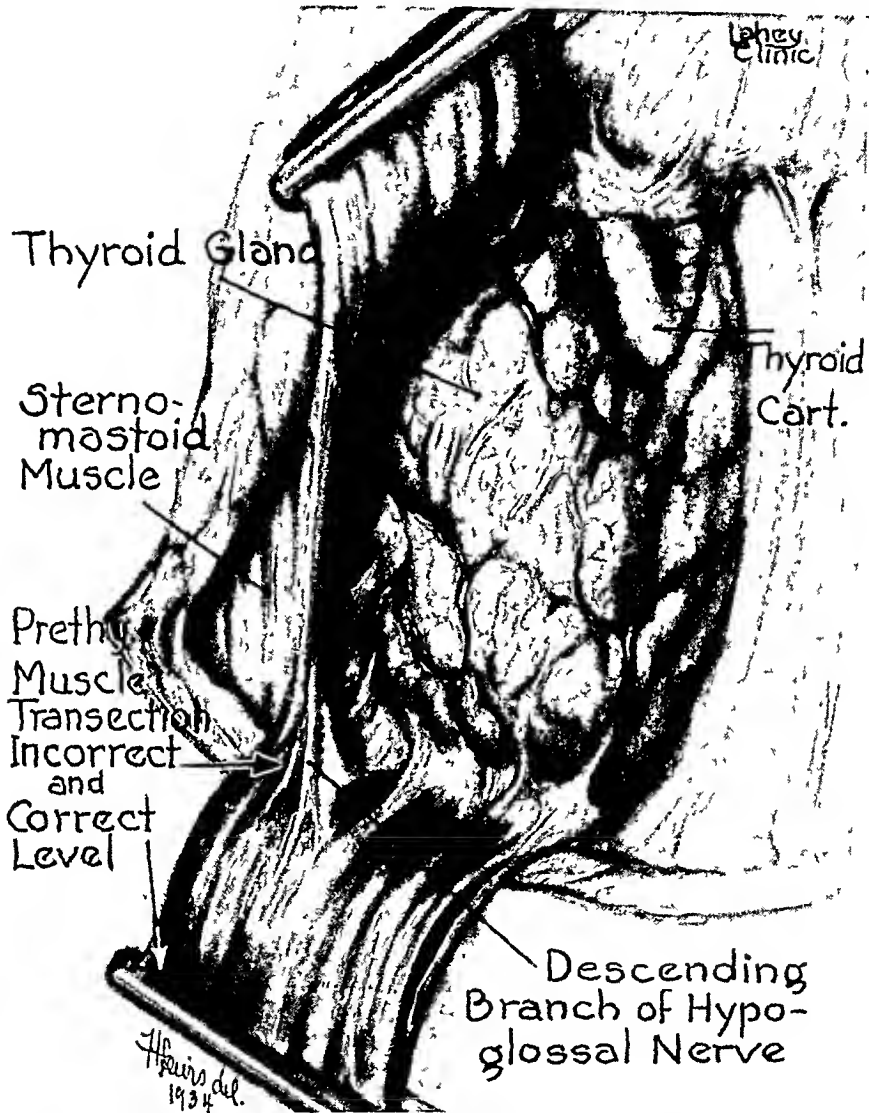


FIG 14.—Innervation of the prethyroid muscles by the descending branch of the hypoglossal nerve at the point at which it is injured when the incision is incorrectly made at a lower level.

flap in order to get adequate height of exposure. When a skin flap is so elevated, double ligation of the thyroid artery well off the thyroid gland with two ties is possible. This insures against postoperative hemorrhage from the superior thyroid artery, a most troublesome hemorrhage, since when a ligature on the superior thyroid artery slips, the bleeding vessels retract up into the fascial plane of the neck, and it is most difficult to clamp and control them without wide exposure. This clear exposure by high elevation

GOITER INCISIONS

Volume 117
Number 3

of the skin flap is important as lack of it, I am certain, has resulted sometimes in inadequate exposure of the upper pole and inaccurate ligation of the superior thyroid artery. A tie about the superior thyroid artery that includes also the tip of the thyroid gland when the skin flap has not been elevated enough to provide a good exposure often shuts off the vessel temporarily but does not permit complete and dependable ligation of the vessel. This frequently permits the patient to cough off the inaccurately applied tie, and results in trying and dangerous postoperative hemorrhage. Such adequate exposure of the superior thyroid vessel with ligation of the superior

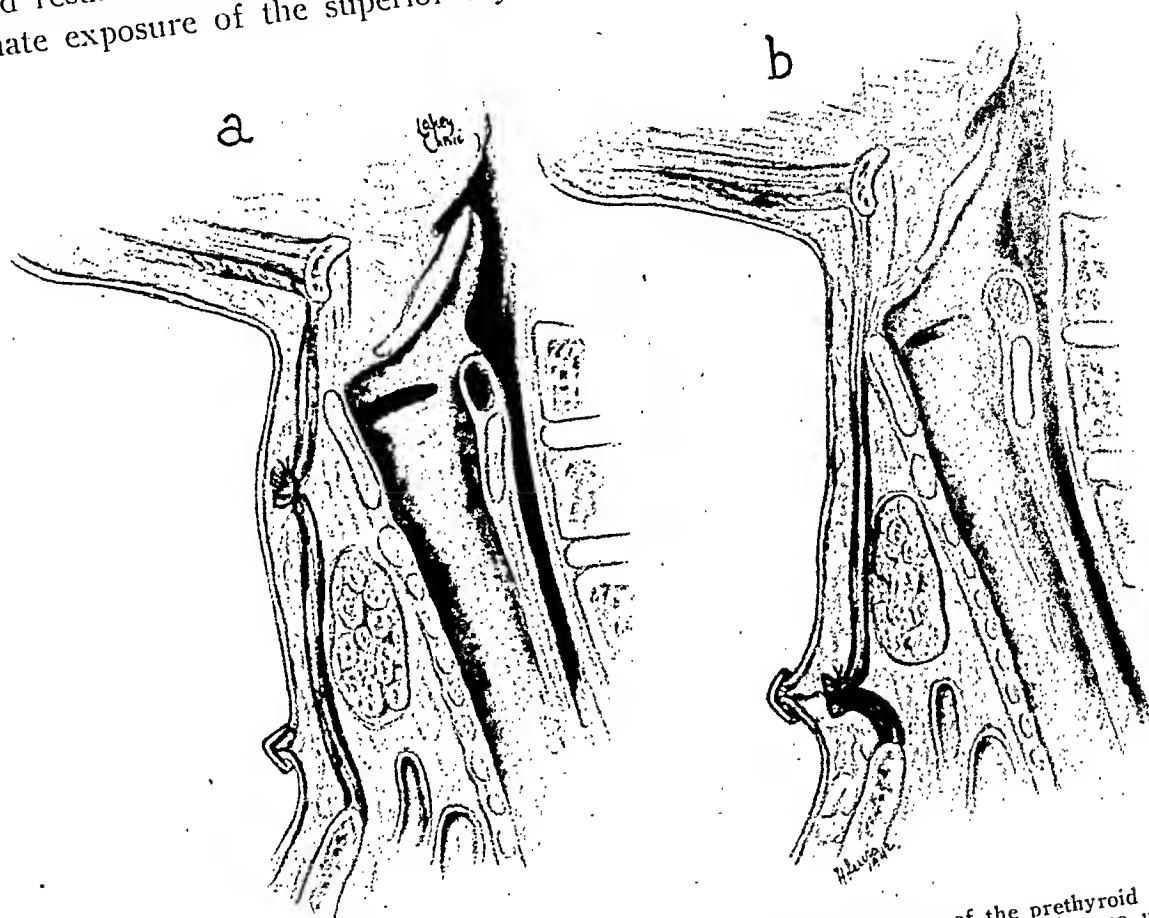


FIG. 15.—(a) A side view of the proper level of transection and suture of the prethyroid muscles. Note the staggering of the high muscle suture and the low skin suture, thus producing no unsightly wound projection or complication. (b) The unfortunate situation which results when the muscles are cut low and muscle suture and skin suture are at the same level.

thyroid vessel well above the tip of the thyroid tissue which forms the upper pole will almost eliminate the possibility of postoperative hemorrhage from the superior thyroid artery.

Should a hemorrhage from the superior thyroid artery occur, unless the bleeding vessel can be seen immediately and plainly on reelevation of the skin flap, one should not waste time in trying to find the vessel in the fascia and muscle plane filled with hematoma. The incision should be extended upward on the side (Fig. 12), the external carotid artery found and the first branch of the superior thyroid artery tied. This procedure, placing, as it does, the patient's life above the beauty of the scar, affords immediate control of

bleeding in a toxic patient sometimes too ill to be submitted to more than one operative procedure for the control of a postoperative hemorrhage.

I know of no surgical procedure which has occasioned greater disagreement and more argument than the question of whether one should cut across the prethyroid muscles, sever them and resuture them, or whether subtotal thyroidectomy should be performed with the prethyroid muscles uncut and retracted to one side. A subtotal thyroidectomy can be undertaken very well without severing muscles, but I personally am not interested in operating upon a patient for thyroid disease without the best possible anatomic exposure of the thyroid and its adjacent and related structures. If an

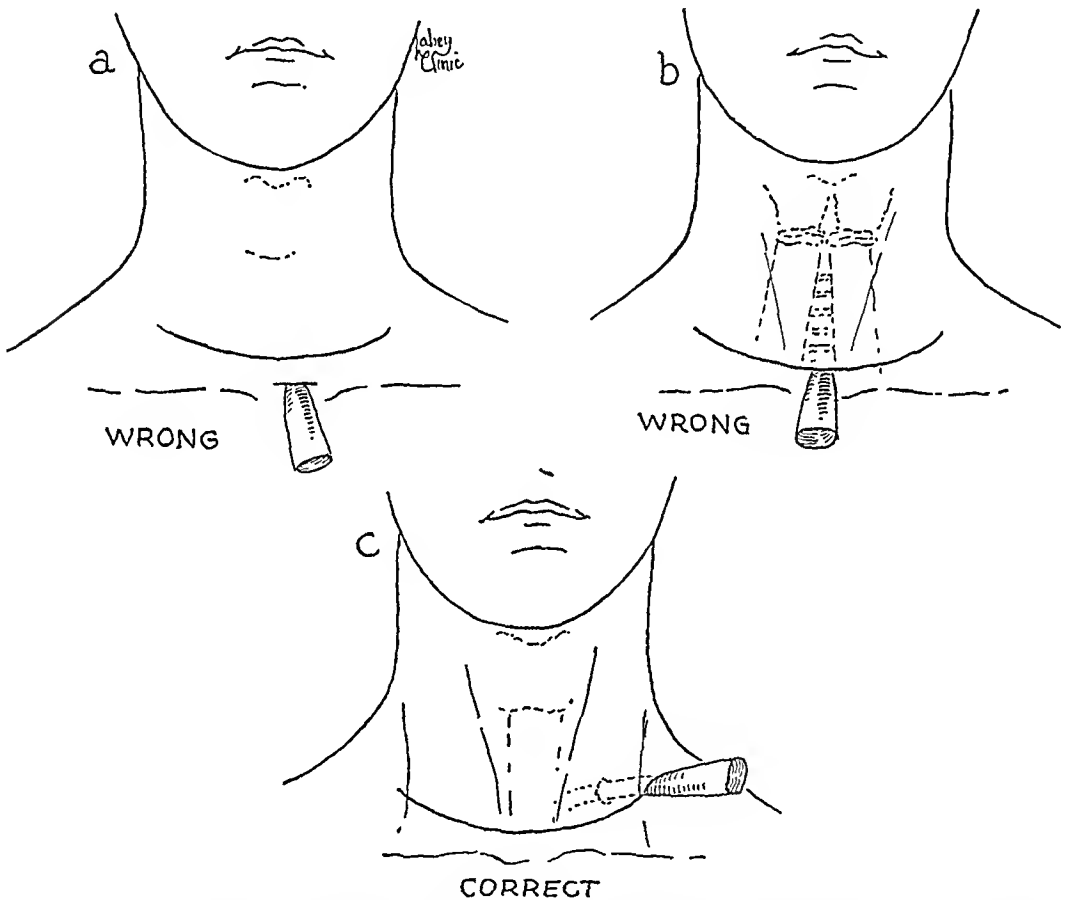


FIG. 16.—(a) The wrong method of drainage. A counter incision for drainage can never be concealed. (b) The drain must pass between the prethyroid muscles when brought out through the central portion of the wound. The skin can become adherent to the trachea when the drain is withdrawn, thus producing upward and downward motion of the scar with swallowing. (c) The proper method of drainage, either through or over the sternomastoid muscle, the drain emerging through the external angle of the wound. With the drain so inserted, the prethyroid muscles can be accurately sutured in the midline, and there are no adhesions between the skin and trachea.

adequate incision is essential in order to obtain exposure for a cholecystectomy, hysterectomy or nephrectomy, it is doubly necessary for a successful subtotal thyroidectomy. Many operations for hyperthyroidism involve risk of the patient's life. Anything which facilitates the exposure adds to the ease of execution of the operation and makes easier the determination of what proportion of the entire thyroid gland is to be removed, and by demonstration of its anatomic relation to the parathyroids and recurrent lary-

geal nerves, adds greatly to the ease and success with which these structures can be preserved. We have demonstrated, conclusively, that if the prethyroid muscles are cut and sutured high there is no functional disability and no disfigurement. If I must choose between cut muscles which can be sutured satisfactorily and a greater hazard of injury to a parathyroid or a recurrent laryngeal nerve with the muscles uncut, I will, and have, consistently chosen the former.

Because we have performed so many operations upon toxic goiters in two stages, we have had the opportunity to cut the muscles on one side, sew

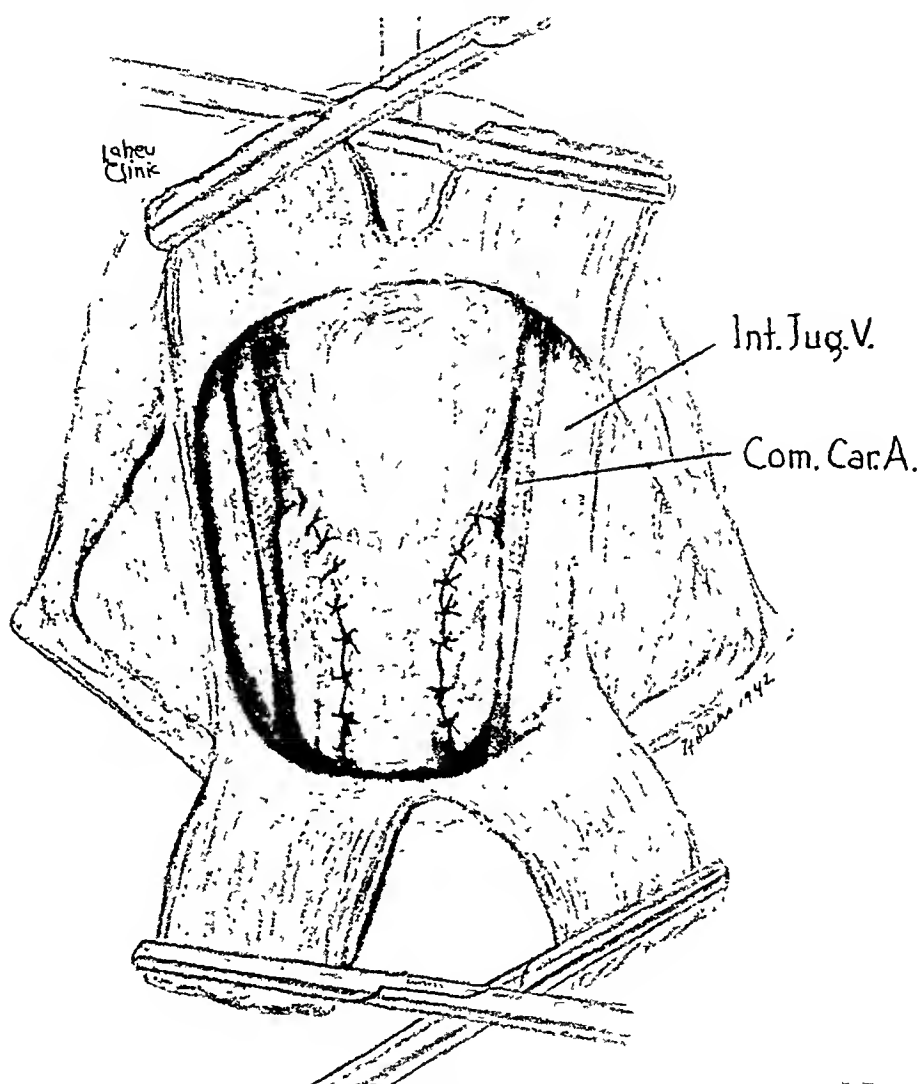


FIG. 17.—The method, which we have repeatedly demonstrated, of suturing the remaining stump of thyroid against the trachea to overcome oozing and thus permit closure of the wound without drainage.

them together, have the patient back at the end of six weeks for the second stage (left subtotal hemithyroidectomy) and observed the condition of the muscles. Invariably one can hardly find the place where the muscles have been sutured, if the incision is made high so that innervation is not disturbed and there is no disfigurement or disability (Fig. 13). The two essential features involved in transection of the prethyroid muscles, in order to obtain better exposure, are that they must be incised high and sutured high,

well up under the upper portion of the wound (Figs. 13 and 14). This avoids denervation of the prethyroid muscles, and, most importantly, staggers the muscle sutures high up under the skin flap (Fig. 15 a) and not low on the same level with the skin incision (Fig. 15 b). The easiest level at which to transect the prethyroid muscles is low, where the nerve innervation is endangered, and where the muscle suture rests close to, or immediately beneath, the skin incision (Fig. 15 b). This error tends to produce unfortunate wound complications and to make undue prominence from the double line of sutures of skin and muscle directly beneath the skin incision.

I am sure that high severing of the prethyroid muscles, clamped well out beneath the sternomastoid, which has been freed and pulled back, has resulted in infinitely better exposure, in drier fields, more anatomic dissections, and more radical dissection, and has resulted in neither organic dysfunction nor disfigurement.

In closure of the skin wound the prethyroid muscles must be sutured accurately and without tension. The muscles in the midline are best brought together with interrupted sutures, making certain they are accurately approximated between the skin flap and the trachea, thus serving to prevent the trachea from becoming adherent to the skin.

If drains are inserted, no counterincision should be made beneath the skin incision through which the drain is to emerge (Fig. 16 a) because this produces an ugly scar which cannot be covered by a necklace. Likewise, if a drain is inserted, and they are rarely employed at this Clinic, it should be brought out at the external angle of the wound either through the belly of the sternomastoid (Fig. 16 c) or in front of the sternomastoid between it and the sutured prethyroid muscles. This brings the drain out through the corner of the incision where the skin incision cannot become adherent to the trachea. If the drain is brought out in the midline between the prethyroid muscles (Fig. 16 b), these muscles gap and the organized scar which fills the hole between the prethyroid muscles when the drain is withdrawn, permits the trachea to become adherent to the skin, making the scar "bob" up and down when the patient swallows. It is well to bear in mind, however, that if bleeding is painstakingly controlled and if the cut surface of the thyroid is turned against the trachea and sutured there, as we have repeatedly advised (Fig. 17), rarely, except in the large intrathoracic goiters is it necessary to use drains. With wound closure without drainage we have had no more accumulation of serum in the wound than when drains were employed.

Finally, for many years, in closure of the skin we have employed no subcutaneous sutures in the platysma. Omitting the suturing of the platysma muscle in no way results in spreading of the scar, as we have also proved by experience with many patients in whom no platysma sutures have been employed.

The skin, closed as it is without drainage, is approximated accurately with clips. The care taken in accurately placing cut skin edges together with clips plays a great part in the appearance of the scar. If the upper

GOITER INCISIONS

edge of the cut skin is permitted to overlap the lower or the cut edges are at all inaccurately approximated, definite thickening of the scar will result. Clips are put fairly close together to control skin oozing, and most importantly, one-half of the clips are removed on the second day and the other half on the third. As a matter of fact, if one wishes, they can all be removed on the second day. There is not the slightest danger of the patient pulling the skin edges apart, because if he elevates the chin he pulls on the sutured prethyroid muscles and does not exert pressure on the skin wound. If skin clips are left on for longer than three days, pressure necrotic spots will develop and result in white dot scars, thus permanently disfiguring the wound.

CONCLUSIONS

Deductions drawn from over 22,000 goiter incisions are presented. In my opinion, however illogical it seems, and even though the physical improvement may be striking, nothing plays a greater part in the happiness of a patient operated upon for goiter than the postoperative appearance of the incision. Technical points which I have found useful in making better goiter incisions and obtaining better scars are discussed.

THE PRE- AND POSTOPERATIVE USE OF A METAL-TIPPED GASTRODUODENAL TUBE AS AN AID IN THE SURGICAL TREATMENT OF DUODENAL OBSTRUCTION IN THE NEWBORN

E. P. MARIS, M.D., A. C. MCGUINNESS, M.D., H. F. LEE, M.D.,
JONATHAN E. RHOADS, M.D., AND T. ALTER ESTELL LEE, M.D.

PHILADELPHIA, PA.

FROM THE CHILDREN'S AND THE PENNSYLVANIA HOSPITALS OF PHILADELPHIA, AND THE DEPARTMENT OF PEDIATRICS, SCHOOL OF MEDICINE, UNIVERSITY OF PENNSYLVANIA

CONGENITAL OBSTRUCTIONS of the duodenum have always presented a difficult surgical problem, and the mortality has remained high in spite of numerous changes in treatment. Ladd has made an important contribution to the field by showing that most of those obstructions due to extrinsic causes are associated with faulty rotation of the large bowel with or without volvulus of the midgut.

It is evident, in reviewing statistics on this subject condensed from Ladd and Gross¹ (Table I), that the mortality of intrinsic obstruction has remained much higher than that experienced from extrinsic obstruction since the introduction of Ladd's operation for the latter. It also seems evident, from the figures cited, that anastomosis is extremely hazardous in the infant and that the lower in the bowel anastomosis is performed the greater the danger. Whether the high mortality associated with simple enterostomy is due to the danger of opening the bowel or whether it is due to the great difficulty of supportive treatment after these procedures, is not clear from the statistics. One of us (W. E. L.) has performed jejunostomy with success in two newborn infants.

It seems possible, therefore, that a small opening in the bowel is not as dangerous as has sometimes been believed, but that the mortality associated with enterostomy has been due to metabolic disturbances and to the selection of patients with poor vitality for this procedure.

TABLE I
MORTALITY IN CONGENITAL STENOSIS AND ATRESIA OF THE SMALL BOWEL, COMPARED WITH THE MORTALITY IN CONGENITAL OBSTRUCTION OF THE DUODENUM DUE TO EXTRINSIC CAUSES

Condensed from Ladd and Gross							
	Jejunostomy or Ileostomy		Gastro-enterostomy		Entero-enterostomy		
	No. of Cases	Mortality Per Cent	No. of Cases	Mortality Per Cent	No. of Cases	Mortality Per Cent	
Stenosis of duodenum.....	1	100%	2	50%	7	72%	
Atresia of duodenum.....	0	—	1	—	4	100%	
Stenosis of jejunum.....	0	—	2	50%	—	—	
Atresia of jejunum.....	0	—	2	—	6	50%	
Stenosis of ileum.....	3	100%	0	—	4	50%	
Atresia of ileum.....	22	100%	0	—	12	75%	
	—	—	—	—	—	—	
• Total.....	26	100%	7	50%	33	70%	
(intrinsic obstruction)							
Total of all intrinsic obstruction.....	64 cases		16 lived, or 75 per cent mortality.				
Total of all extrinsic obstruction.....	44 cases		27 lived, or 38 per cent mortality.				
Total of extrinsic cases treated by Ladd's method....	35 cases		27 lived, or 23 per cent mortality.				

DUODENAL OBSTRUCTION IN NEWBORN

A difficulty which we believe may contribute to the mortality in this group of patients is that of being sure that no intrinsic obstruction remains after adhesions have been released. The duodenum is to some extent bound down normally, and when it becomes dilated its fibrous attachments become taut and compress it. When these attachments are divided, the bowel seems to be released and the area of dilatation may even appear to advance slightly.

There is another situation which may lead to the termination of an operation before the lumen of the duodenum is clear. It is possible for the small bowel to be obstructed by two or more diaphragms (Fig. 1). After the release of the first obstruction bowel contents start to pass but may not be followed far enough to reveal the next obstruction.

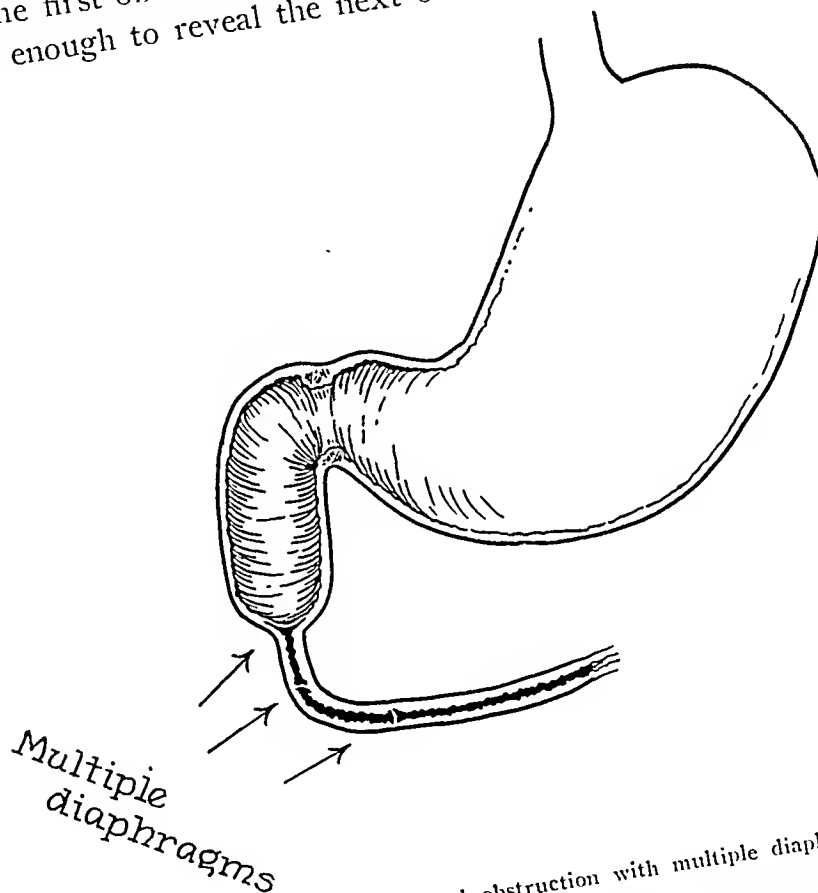


FIG. 1.—Diagram showing duodenal obstruction with multiple diaphragms.

Therefore, we have found it to be a useful maneuver to introduce a special tube into the duodenum before operation, which has a metal tip large enough to be grasped and manipulated through the bowel walls. The stomach is emptied *en route*. In cases of duodenal obstruction all possible extrinsic causes should be excluded by freeing the duodenum throughout its length, after the right side of the colon has been reflected to the midline or beyond, taking care to avoid injury to the mesenteric vessels, when it will be possible to free the duodenojejunal flexure so that the duodenum is relatively mobile for its full length from the pylorus to the ligament of Treitz. The tip of the tube is then manipulated as far as the proximal jejunum. If any intrinsic obstruction is present, it should be readily detected. In the event that the obstruction is due to a diaphragm, a small opening can be made

with a transverse incision through the antimesenteric border of the bowel, at a point one to two inches below the obstruction, through which a hemostat, can be inserted as in Fig. 2 to grasp the metal tip of the tube (and the diaphragm) and thus tear or bite an opening through the diaphragm and draw the tube four or more inches into the lumen of the bowel distal to the obstruction. Subsequently, the incision in the bowel wall is closed transversely with two layers of sutures.

The following four case reports illustrate the use of such tubes:

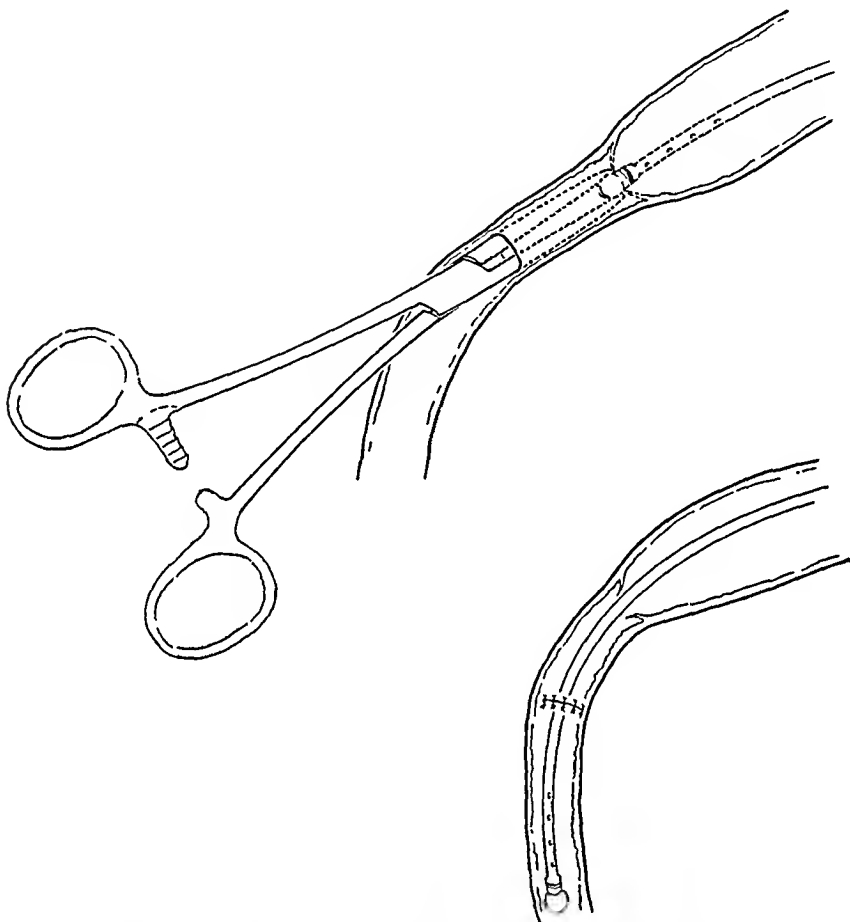


FIG. 2.—Method of destroying duodenal diaphragms employed in Cases 1 and 4. The only opening in the bowel is small, antimesenteric, and is placed below the obstruction through normal bowel wall. It is closed transversely.

ILLUSTRATIVE CASES

Case 1.—Baby S. T. A., a female infant, regurgitated bile-stained material from birth. Roentgenologic examination, at the age of four days, showed dilatation of the stomach and duodenum but practically no air in the remainder of the intestinal tract (Fig. 3). An operation under ether anesthesia revealed numerous tight fibrous bands across a distended duodenum. These were released. The collapsed bowel did not fill-out much but it was thought that it did increase in diameter slightly. The condition of the child being critical, the abdomen was closed.

Vomiting continued, and roentgenologic examination, made three days after operation, again showed an absence of air in the intestine. A brass-tipped gastrooduodenal tube (No. 10 F.) was then manipulated as far as the duodenum under fluoroscopic guidance and the wound reopened. An attempt to pass the tube along the duodenum revealed, by palpation and visualization of the brass tip, the presence and location of a

DUODENAL OBSTRUCTION IN NEWBORN

diaphragm. This was then destroyed, as shown in Figure 2, and the tube drawn about three inches into the lumen of the jejunum. Following this operation the baby began to have yellow stools and gradually to gain weight. Roentgenologic examination a few days later showed a considerable quantity of gas in the intestine (Fig. 4). The patient

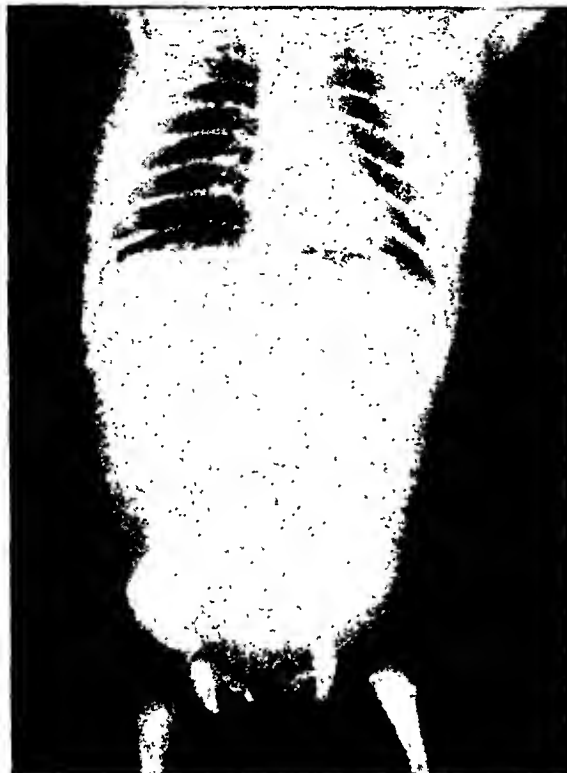


FIG. 3.—Case 1: Roentgenogram of Baby S. T. A. before relief of the obstruction.



FIG. 4.—Case 1: Roentgenogram of Baby S. T. A. after relief of the obstruction.

was discharged from the hospital, in good condition, four weeks later, and reached normal weight at the end of the third month.

The conditions encountered in Case 1 are shown diagrammatically in Figure 5.

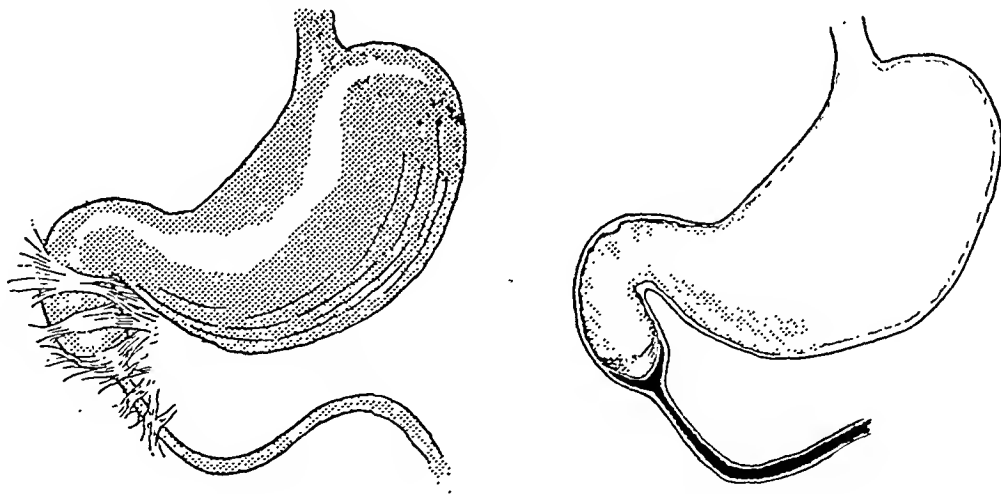


FIG. 5.—Diagram of the operative findings in Case 1.

Case 2.—Baby S. T. I., a male infant, vomited greenish material from birth. Roentgenologic examination, with barium, showed duodenal obstruction. Prior to operation the brass-tipped gastroduodenal tube was passed. In this infant adhesions over the second portion of the duodenum had to be divided. It was again found difficult to pass the tube into the distal duodenum but it finally slipped through a strictured area, and some three inches of the tube was left in the proximal jejunum. Subsequently, six hours later, the tube had to be removed because of gagging and respiratory em-

barrassment, but, nevertheless, the child began to pass stools within 24 hours and he has gradually gained weight and strength, and his bowels were functioning normally three weeks postoperatively. At six months of age he weighs 17 pounds, has the usual diet and has reached the normal level of development.

Case 3.—Baby A. G., a female child, was admitted to the Children's Hospital because of persistent vomiting of bile-stained material. Operation was deferred until the 27th day of life because the obstruction was not complete. After conservative treatment during this period had failed to result in improvement, operation was undertaken,



FIG. 6—Case 4. Marked dilatation of the duodenum at the age of two years.

with the aid of a No. 10 F. brass-tipped duodenal tube. The duodenum was found to be dilated and rather tight bands passed over it near the duodenojejunal flexure. After the right half of the colon was reflected to the midline, these bands were divided. It was then found that some of the small intestine had become adherent on the lateral side of the mesentery of the ascending colon. The brass-tipped tube was of decided value in determining the patency of the duodenum in the confusing anatomic anomalies found at operation.

After freeing all of the abnormal bowel attachments, the abdomen was closed and, except for respiratory difficulty necessitating removal of the tube during the period of reaction from anesthesia, a satisfactory convalescence followed.

Case 4.—Baby R. J. L., a two-year-old female child, was admitted to the Children's Hospital on account of recurrent episodes of vomiting. The vomitus was usually bile-stained. Roentgenologic examination showed evidence of partial obstruction in the descending portion of the duodenum, with an extreme degree of dilatation (Fig. 6).

At operation, the duodenum was exposed by reflection of the colon and a No. 12 F. Miller-Abbott tube, which had been previously introduced, was moved as far down the duodenum as possible. In the last portion of the duodenum the tip was deflected toward the mesenteric side by a shelf of tough fibrous tissue. Here it caught in a pocket and could not be advanced further.

The bowel was opened below the obstruction and along its antimesenteric border, as in Case 1, and the tip of the tube, together with the walls of the diaphragm, were seized with a hemostat. As they were drawn down and through the incision in the duodenal wall the diaphragm was incised, and the brass tip and tube drawn into and left several inches in the lumen of the jejunum. The opening in the bowel was closed transversely.

Convalescence was satisfactory, and the patient's symptoms were relieved immediately. In this case, had it not been for the tube, an anastomosis probably would have been necessary. With this patient the tube remained in the jejunum for three weeks, and was used for feeding.

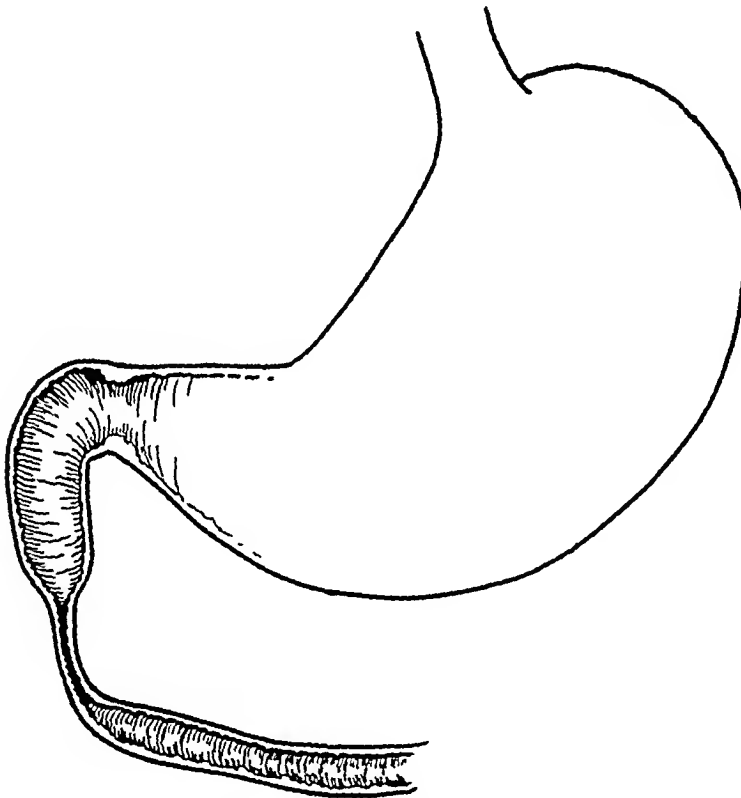


FIG. 7.—Narrowing of the duodenum without complete obstruction. This condition was found in Case 2.

DISCUSSION.—In attacking the problem of congenital duodenal obstruction, it is desirable to avoid anastomosis and to open the bowel as infrequently as possible. When it is necessary to open it, the incision should be as short as possible, and should preferably be made through normal bowel wall at a point where it will not interfere with the blood supply of adjacent portions.

A duodenal tube, such as is shown in the insert in Figure 2, may perform four functions. It is employed, first, to deflate the stomach. Next, when followed fluoroscopically, it may give additional evidence on the point of the obstruction. Third, it is available at the time of operation to test the patency of the duodenum after the latter has been freed. Fourth, it makes possible the destruction of a diaphragm, by the method illustrated in Figure 2.

This method fulfills the criteria outlined above rather well, and should entail a relatively small risk of peritonitis.

A word of caution is necessary in regard to the employment of the gastroduodenal tube during the early postoperative period. The two-year-old child was not disturbed by the presence of the tube at this stage. All three of the newborn infants, however, each of whom tolerated the tube well preoperatively and during the operation, showed evidence of serious respiratory difficulty, and a condition resembling shock at some time during the period of reaction from anesthesia. Prompt removal of the tube resulted in relief in each instance. From our experience, it would seem advisable to remove the tube before complete reaction from the anesthesia takes place. Eighteen to 24 hours postoperatively the tube has been reinserted, for relief of distension, without the recurrence of unfavorable signs.

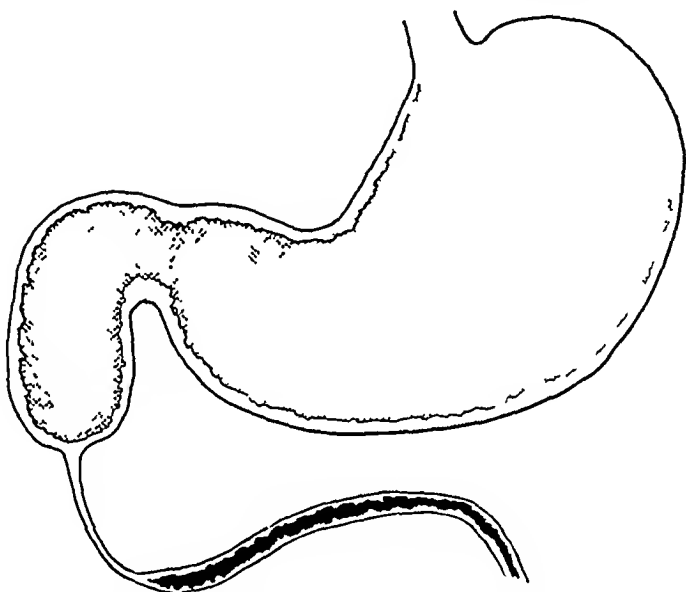


FIG 8—Complete atresia of the duodenum requiring gastrojejunal anastomosis.

If no diaphragm is present and only a stenosis is found, it may be possible to pass the tube through the narrowed area, as in Figure 7. In certain cases an atresia of a considerable segment of bowel is present (Fig. 8). In these cases there would seem to be no alternative other than to perform an anastomosis.

CONCLUSION

A duodenal tube with a metal tip of sufficient diameter to be visualized and grasped through the bowel, is recommended as an adjunct in operations for relief of congenital duodenal obstructions.

Its use in four cases is described which are illustrative of its value.

We wish to acknowledge our indebtedness to Dr. Paul Bishop and Dr. Ralph Bromer for the roentgenograms, and to the Harrison Department of Surgical Research, University of Pennsylvania, for assistance with the illustrations.

REFERENCE

- ¹ Ladd, W. E., and Gross, R. E.: *Abdominal Surgery of Infancy and Childhood*. W B Saunders, Philadelphia, 1941.

CONGENITAL CYSTIC DILATATION OF THE COMMON BILE DUCT*

CASE REPORT AND REVIEW OF LITERATURE†

THOMAS A. SHALLOW, M.D., SHERMAN A. EGER, M.D.,

AND

FREDERICK B. WAGNER, JR., M.D.

PHILADELPHIA, PA.

THE UNIQUE ASPECTS of congenital cystic dilatation of the common bile duct, otherwise known as choledochus cyst, make it interesting, notwithstanding its rarity. The relatively few reports in the literature warrant the accumulation of all the available data in order to arrive at a thorough understanding of this subject. With this in mind a complete review of the literature is made and a case report is included.

The outstanding features of the case, herewith cited, are as follows: The condition was suspected preoperatively, and peritoneoscopy was undertaken as an adjunct in diagnosis. The cyst was extirpated and right and left hepaticoduodenostomy performed over No. 18 F. catheters. The latter were removed through a gastroscope by Dr. Clerf during a second hospital admission, 11 weeks postoperatively. Recovery ensued.

Case Report.—P. W., white, male, age 20, was admitted to the ward medical service of the Jefferson Medical College Hospital July 11, 1941. The chief complaints were pain in the right upper abdomen, a mass in the same area, jaundice, and fever.

The patient had been well until November, 1940, at which time he experienced his first attack of pain in the right upper abdomen. The pain was definitely localized at the right rectus-costal margin junction; it was sharp, did not radiate, and lasted for three to four days, with acute exacerbations seven or eight hours apart. This pain was followed within 24 hours by a mass in the same area, jaundice, and slight fever. He was studied for one week at his College Infirmary and discharged to the care of his family physician, with a diagnosis of catarrhal jaundice. During the following month the jaundice and fever gradually disappeared, but weakness persisted, and he was advised to remain out of college in order to regain his strength.

From December, 1940 to June, 1941 the patient remained at home and performed small chores. The mass in the right upper abdomen persisted, but without pain, jaundice, or fever. He ate an ordinary diet and took no drugs.

About two weeks prior to admission, the patient again experienced pain in the right upper abdomen, which had the same characteristics previously noted; it lasted for eight hours and was severe enough to force him to bed. The pain was again followed, as in the previous attack, by jaundice and fever. With each attack of jaundice the urine became darker than usual, and the stools were of a light brown color, but not clay-colored. There was a loss of seven to eight pounds in weight with each attack, but this was subsequently regained, and the weight on admission was that normally noted. Vomiting did not occur at any time. A review of all the remaining systems revealed a normal history. His past medical history was uneventful, and the family history failed to reveal any member ever suffering from similar complaints.

* Presented before the Philadelphia Academy of Surgery, December 7, 1942.

† From the Samuel D. Gross Surgical Division of the Jefferson Medical College Hospital.

Physical Examination.—The patient was a well-developed, slightly undernourished white male, who appeared chronically ill. Temperature 99.4° F.; pulse 76; respirations 20. Blood pressure 112/70. Weight 143 pounds. He had slight pallor and a greenish tinge to the skin. The scleras were markedly jaundiced. The tongue was coated and a few tonsillar tabs were present on the left side. There was slight anterior cervical lymph node enlargement. The heart and lungs were essentially normal. There was prominence of the superficial veins over the right lateral chest wall. A large, globular mass, about six inches in diameter, was visible in the right upper quadrant of the abdomen, which moved on respiration toward the midline and very slightly downward. It was firm and smooth on palpation, and no definite edge could



FIG 1.—Plain film of the abdomen showing the faint outline of the mass

be made out. There was a resistance to the palpating hand from the right anterior superior iliac spine across the navel to the left costal margin, which was suggestive of hepatic enlargement; percussion note over this area was flat. The remainder of the physical examination was essentially normal. *Diagnostic Impression:* Abdominal mass with obstructive jaundice.

Laboratory Data and Special Studies.—Examination of the blood showed: Hemoglobin 65%; red cells, 3,720,000; white cells, 5,600, with polymorphonuclear cells 48%, lymphocytes 46%, and monocytes 6%. Color index 0.88.

Urinalysis, repeated at intervals of several days, showed deep green color (grossly bile-stained); reaction sometimes acid, sometimes alkaline; specific gravity ranging between 1.009–1.027; albumin varying from none to moderate amounts; sugar, negative; occasional triple phosphate crystals; no red blood cells; pus cells absent in some specimens, and present up to 30 per low power field in others; no casts. Test for presence

of bile pigment was strongly positive in three different specimens. Test for urobilinogen was positive in three different specimens in dilutions varying from 1-5 to 1-40.

Stool examination revealed a normal amount of bile pigment present.

Wassermann and Kahn serologic studies were negative.

The sedimentation rate was rapid, with a fall to 31 mm. within one hour.

Blood sugar (fasting) was 77 mg. Glucose tolerance test revealed a fasting sugar of 72; $\frac{1}{2}$ hr. 128; 1 hr. 113; 2 hrs. 63.

Serum cholesterol was 163 mg. and one week later 173 mg.

Serum phosphorus was 3.6 mg. and serum phosphatase 21.4 Bodansky units.

Serum proteins were 6.23 Gm., with albumin 3.46 Gm. and globulin 2.77 Gm.

Prothrombin times taken several days apart and during treatment were 38%, 40%, 63%, 87%, and 66%, respectively.



FIG. 2.—Gastro-intestinal series showing displacement of stomach and jejunum.

Bromsulfalein test showed 15% of dye retained, and the test repeated one week later showed 20% dye retained.

Van den Bergh test showed a positive direct reaction, with serum bilirubin of 3.5 mg. The same test repeated one week later again showed a positive direct reaction, with serum bilirubin of 4.6 mg.

Hippuric acid test showed an excretion of 1.20 Gm. as benzoic acid.

Urea clearance was 85% of average normal.

Circulation time was 15 seconds; venous pressure 100 mm. of water; and vital capacity 4,500 cc.

Biliary drainage revealed occasional cholesterol crystals in the A and B specimens, and none in the C specimen.

Sigmoidoscopic examination was normal.

Roentgenologic Studies.—*Plain film of the abdomen* (Fig. 1): There is a diffuse haze over the upper abdomen which seems to be due to a greatly enlarged liver. The spleen is not visible and both kidneys are normal in size and shape. *Roentgenologic Interpretation:* Enlarged liver.

Cholecystogram: Examination of the abdomen 15 hours after the ingestion of the dye does not show any evidence of a gallbladder shadow. There is a large mass in the right side of the abdomen, a portion of which is enlarged liver. This extends downward as far as the upper portion of the ilium, and it may be that there is a



FIG. 3.—Barium enema showing displacement of the hepatic flexure and transverse colon.

mass which is distinct from the liver. A roentgenogram made three hours later still shows no evidence of dye in the gallbladder. *Interpretation:* Nonvisualization of the gallbladder by oral cholecystography. Large mass on right side of abdomen.

Gastro-intestinal Series (Fig. 2): Fluoroscopy of the chest was negative. The esophagus was negative to barium liquid and paste. The stomach was elongated and markedly displaced to the left. Its greater curvature was one centimeter below the iliac crest. The stomach exhibited smooth indentation along its lesser curvature, apparently due to extrinsic pressure. The rugal pattern was intact. The antrum was flattened and displaced anteriorly and to the left, apparently by extrinsic pressure. There was no evidence of an intrinsic organic lesion of the stomach. The duodenum

CONGENITAL CYST OF COMMON DUCT

was displaced downward and markedly anteriorly, especially in the descending limb. Progress through the descending limb was delayed, apparently secondary to extrinsic pressure. These displacements are apparently secondary to a retroperitoneal mass. It may be a retroperitoneal sarcoma or possibly may arise from the pancreas and represent a pancreatic cyst.

Progress through the small intestine was unretarded. The jejunum, however, was displaced to the left and downward. At one hour the barium was distributed through the stomach, duodenum and jejunum. At two hours and thirty minutes the stomach and duodenum were empty and the barium was distributed through the jejunum and ileum. At four hours and thirty minutes the barium had reached the descending colon. There was noted a displacement downward, of the hepatic flexure and the transverse colon. The terminal ileum appeared negative. There was a sug-



FIG. 4.—Intravenous urogram showing retention of dye in the right renal pelvis, due to pressure on the ureter.

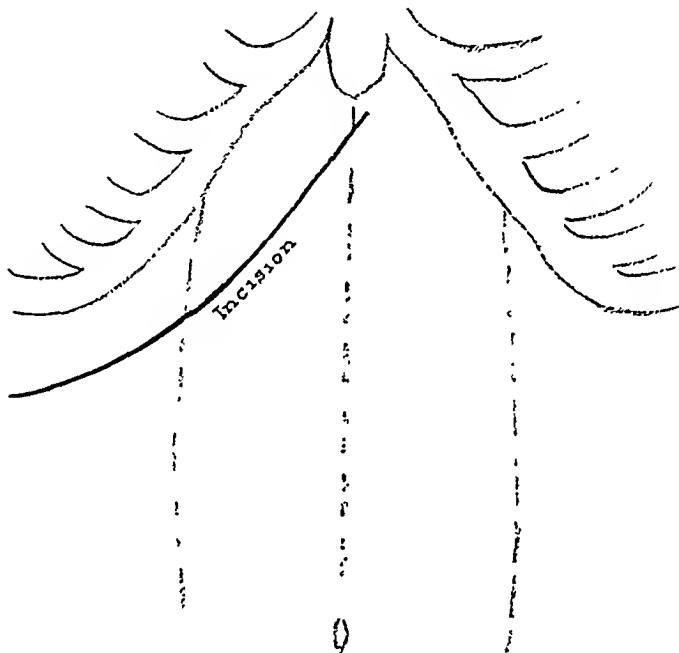
gestion of an incompletely filled appendix. *Interpretation:* Examination of the upper gastro-intestinal tract reveals evidence of extrinsic pressure on the stomach, duodenum, jejunum and colon, apparently due to a right-sided retroperitoneal mass. This may be either a retroperitoneal sarcoma or a pancreatic cyst.

Barium Enema (Fig. 3): The colon was studied following barium injection. The barium flowed readily throughout as far as the cecum. This did not fill readily. The colon was large in size and was displaced downward in the region of the hepatic flexure, apparently by the previously noted extrinsic mass. Except for the cecal region it filled out readily and exhibited no evidence of an organic lesion. However, the cecal area was noted to fill intermittently and when filled, exhibited no evidence

of a defect. Following evacuation there was noted a small residue in the sigmoid and in the cecal region. *Interpretation:* Barium enema study of the colon shows evidence of extrinsic pressure on the hepatic flexure and possibly on the transverse colon. The cecum filled with difficulty; however, no lesion could be demonstrated.

Intravenous Urogram (Fig. 4): Both kidneys are normal in size, shape, and position. The contrast material was normally excreted by both kidneys, and the pelves and calices have a normal appearance. There is a tendency to retention of the contrast material in the upper part of the right ureter. This might be an expression of early pressure by the abdominal mass that is present. However, one hour after injection, practically all of the contrast material had been eliminated from the kidneys. The bladder has a good degree of density and is small in outline. *Interpretation:* Normal appearing and functioning kidneys. The abdominal mass might be beginning to press upon the right ureter.

Peritoneoscopic Examination: This was performed under local 1% novocain anesthesia. The peritoneal areas were well visualized. The only abnormal finding was a



Operative Approach

FIG. 5.—Operative approach to choledochus cyst.

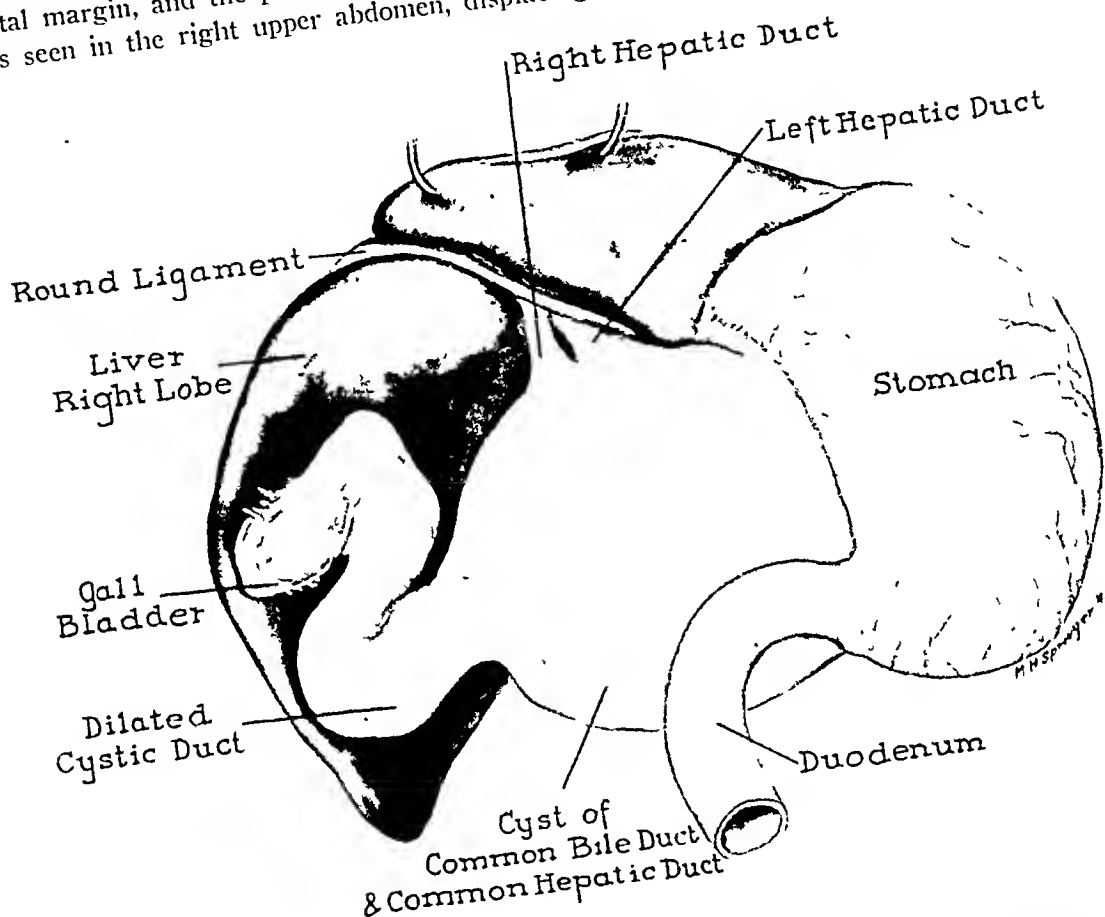
large retroperitoneal mass which displaced the duodenum anteriorly and medially, the liver superiorly, and the hepatic flexure of the colon inferiorly. The mass was circumscribed and was soft, probably of cystic nature. *Impression:* Retroperitoneal mass near the right kidney of cystic nature, possibly a cyst or a polycystic right kidney.

Preoperative Course.—The patient was given a high caloric, high carbohydrate, moderate protein, low fat, high vitamin diet. Because of the low prothrombin time, vitamin K was administered intravenously daily, and with this therapy the prothrombin time approached more nearly the normal levels (see laboratory data). Sodium phosphate was also administered orally each morning. During this time the patient was being studied carefully, the results of which are given under the laboratory data and special studies. A low-grade fever was present, there being usually a slight rise daily from normal to seldom more than 100° F. On July 29, 1941, the patient was transferred to Men's Surgical "A" Service. *Final Preoperative Diagnosis:* Retroperitoneal mass, probably choledochus cyst, with obstructive jaundice.

CONGENITAL CYST OF COMMON DUCT

Operative Procedure: Excision of cystic mass, gallbladder, and cystic duct; implantation of the right and left hepatic ducts into the first portion of the duodenum over No. 18 F. catheters.

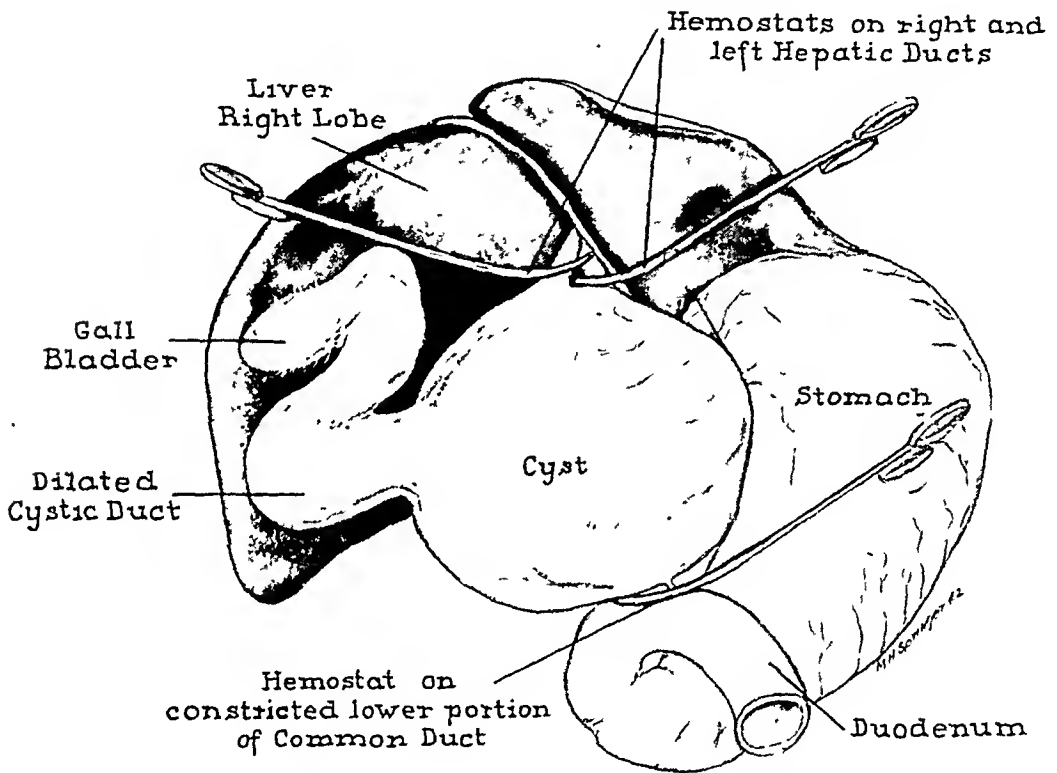
Operation.—July 31, 1941: The patient was given nembutal gr. $1\frac{1}{2}$ at 7 A.M. and 9 A.M., and morphine sulfate gr. $\frac{1}{4}$ at 1 P.M. At 1:30 P.M. pontocaine (16 mg.) spinal anesthesia was administered. Abdomen was then prepared with iodine and alcohol and draped. An incision (Fig. 5) was made one inch below and parallel to the right costal margin, and the peritoneal cavity opened. A large retroperitoneal mass (Fig. 6) was seen in the right upper abdomen, displacing the duodenum medially and anteriorly,



Pathologic condition encountered at Laparotomy

FIG. 6.—Relational anatomy of choledochus cyst. the transverse colon caudally, and the gallbladder laterally. The peritoneal covering was incised and stripped free, thus liberating the mass at all but three points, namely, the duodenum, gallbladder, and under margin of the liver. The cyst was aspirated and found to contain bile, a specimen of which was sent to the laboratory for study. The gallbladder was slightly distended with inspissated bile, and the cystic duct which opened into the lateral portion of the main mass was greatly enlarged. At the upper surface two dilated separate hepatic ducts opened into the mass. The mass itself opened into the duodenum at the ampulla of Vater through a markedly stenosed lower portion of the common bile duct, the lumen of which was about 1.5 mm. The cystic mass with gallbladder attached was removed (Fig. 7). The left hepatic duct was then anastomosed to the first portion of the duodenum (Fig. 8). The details of this procedure are shown in Figure 9. A No. 18 F. catheter was placed in the left hepatic duct for a distance of about one inch and anchored in place with black silk sutures. A small gastrotomy was then performed near the pylorus and a hemostat introduced. An incision was made

in the first portion of the duodenum over the tip of the hemostat equal in length to the diameter of the hepatic duct. The catheter was then pulled through the incision by the hemostat and the hepatic duct was sutured to the duodenum with black silk sutures. With further traction on the catheter by the hemostat the hepatic duct was pulled into the duodenum for about one half inch, and the serosa of the duodenum was sutured to the duct. This procedure was repeated in anastomosing the right hepatic duct to the first portion of the duodenum (Fig. 10). The catheters passed through the pylorus and lay free in the stomach. The gastrotomy was then closed with black silk sutures. Figure 11 is a plain roentgenogram of the abdomen taken postoperatively showing the catheters in place. The peritoncum and the remainder of the wound were then closed in layers around drains. Four heavy black silk stay sutures were introduced.



Extirpation of Cyst and Gall Bladder

FIG. 7.—Extirpation of choledochus cyst and gallbladder, showing clamps on bile ducts before division.

After one hour and fifteen minutes the anesthesia was supplemented by cyclopropane and ether inhalation by the closed Heidbrink method. The total operating time was two hours and fifteen minutes. The patient left the operating room in good condition. Figure 12 shows the specimen removed at operation.

Pathologic Examination.—*Gross:* Specimen A consists of a large cyst, 15 cm. in diameter. The wall is greenish-yellow, inelastic and fibrous. It contains serosanguinous fluid. There are no papillae.

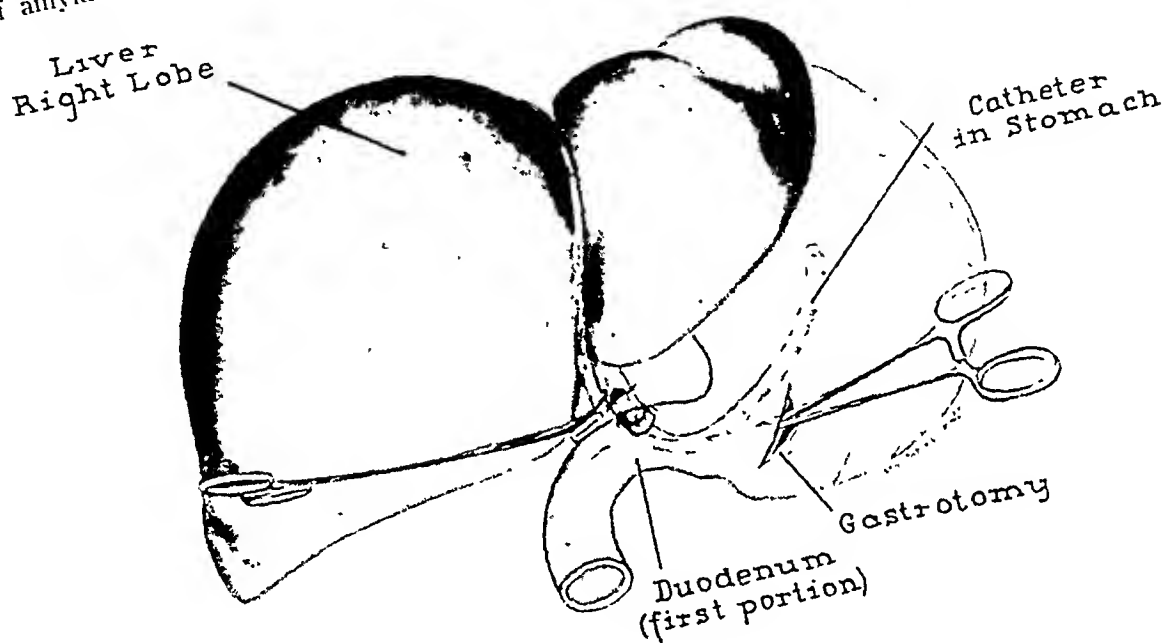
Specimen B consists of a gallbladder, measuring 8 x 5 cm., to which the cystic duct, 5 cm. in length, is attached. The gallbladder is thickened and fibrosed and the mucosa is necrotic. It contains greenish, purulent liquid, and no calculi.

The cystic duct is dilated to one centimeter in diameter in certain sections. It is tortuous and its wall is thick and fibrotic. No section of the duct was taken as the specimen is for the museum.

CONGENITAL CYST OF COMMON DUCT

Histologic Examination: Sections of the gallbladder wall are lined with normal columnar epithelium. Many of the cells contain droplets of secretion. The submucosa is moderately edematous, contains many blood vessels and is infiltrated with plasma and round cells. The muscle coats also contain some degree of inflammatory infiltration. Sections of the common duct (Fig. 13) show a denudation of their mucosa. The mucosal surface is covered with a few plasma cells and lymphocytes. The wall is markedly thickened and composed of dense fibrous connective tissue. There is no evidence of malignancy in any of the sections. **Pathologic Diagnosis:** Marked dilatation of the common duct, cystic duct, and gallbladder; chronic cholangitis; chronic cholecystitis.

Examination of bile removed from the cyst: Material contains a moderate amount of amylase.



Anastomosis of left Hepatic Duct to First Portion of Duodenum

FIG. 8.—Left hepaticoduodenostomy aided by gastrotomy.

Postoperative Course: Aside from the fact that there was rather profuse drainage of bile for a time through the incision, the convalescence of the patient was uneventful. The patient required considerable vitamin K, and in spite of administration several times daily intravenously, the prothrombin level was 25% on the third day postoperatively, 48% on the seventh day, and 52% on the twenty-fifth day. The blood count postoperatively revealed a hemoglobin of 55%; red cells, 2,660,000; and white cells 8,900; color index 1.01. Two blood transfusions of 500 cc. each were given the first week postoperatively. The blood count subsequently rose and just before discharge from the hospital the hemoglobin was 77%; red blood cells, 3,200,000; white blood cells 9,300; color index 1.09.

Routine urinalyses were normal except for an occasional trace of albumin. On the twelfth day the urine was positive for bile pigment and positive for urobilinogen in dilution of 1-40. The color of the stools was normal. On the eleventh day, liver function studies revealed all dye removed (bromsulfalein

test); positive direct van den Bergh reaction; serum bilirubin, 3.4 mg.; and serum cholesterol was 145 mg.

On the seventeenth day, liver function studies revealed 20% dye retained; positive direct van den Bergh reaction; and serum bilirubin 1.6 mg.

A roentgenogram of the abdomen on the eighteenth day revealed two pieces of rubber tube present in the upper left abdomen, the upper ends being on a level with the twelfth thoracic vertebra and the lower ends extending down to the level of the fourth lumbar vertebra. This study was repeated on the thirty-third day and showed that the two pieces of rubber tube mentioned previously were still present in the upper left abdomen and coincided with the gas shadow of the stomach and were probably within the stomach. They occupied the same position as in the last examination.

On September 6, 1941 (37th day postoperatively), the patient was discharged as improved. Jaundice had disappeared, the operative site was well healed, and the patient asymptomatic. He was instructed to return in six weeks for further study and removal of the tubes.

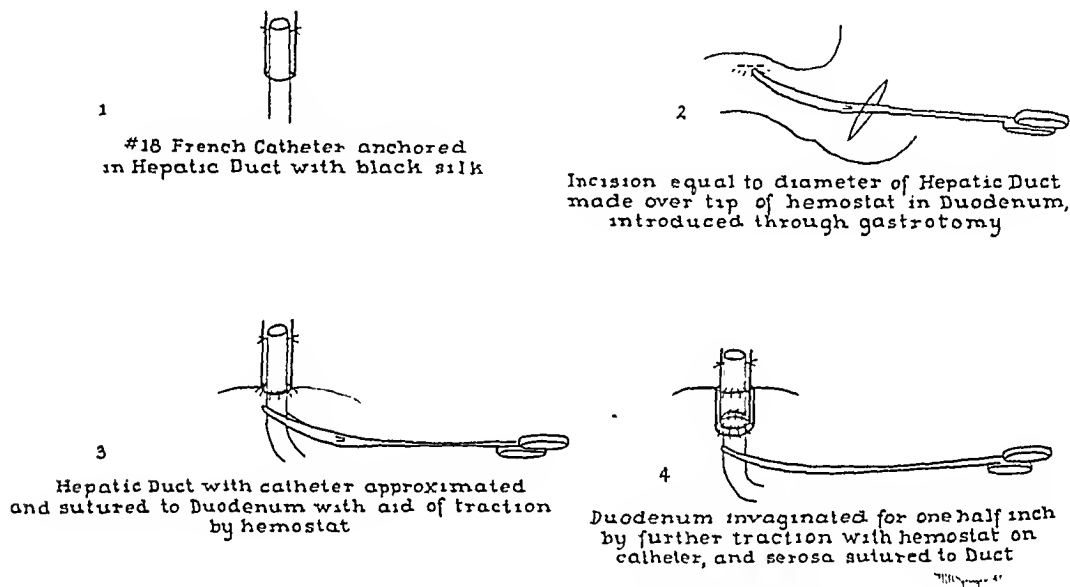


FIG. 9.—Steps employed in hepaticoduodenostomy.

Second Hospital Admission.—The patient was readmitted October 20, 1941. He stated that he had felt well since his discharge from the hospital. The presence of the tubes in his stomach did not cause him distress of any kind. His appetite was good, and he had gained three pounds weight. His weight on this admission was 146 pounds. His bowels were regular and the stools were normal in consistency and color. The remainder of the systemic review was normal.

Physical Examination.—Except for the healed scar of the previous operation in the right upper abdomen, the physical examination was normal.

Laboratory Data.—Blood count revealed hemoglobin 84%; red blood cells, 4,100,000; white blood cells, 8,100; and color index, 0.98. Urinalyses were normal. Liver function studies revealed 10% dye retained (bromsulfalein test); positive direct van den Bergh reaction; and serum bilirubin 1.3 mg.

Reexamination of the upper abdomen roentgenologically again showed the presence of two tubes which overlay the gas shadow of the stomach and were apparently within this organ. The ends of both tubes were visible and apparently both ends also lay within the stomach.

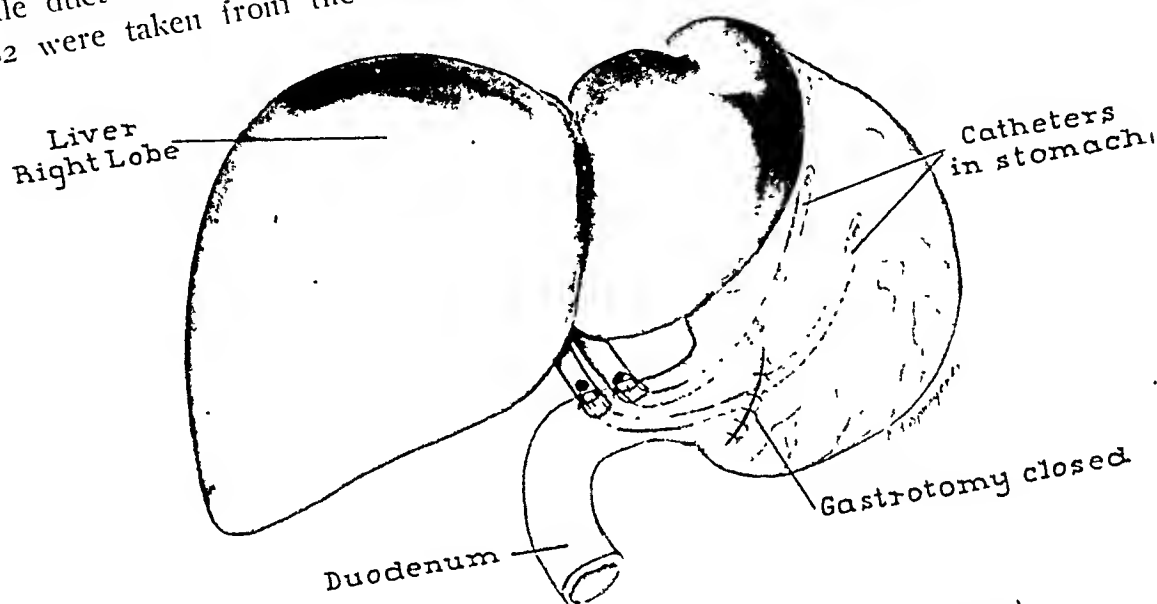
Subsequent Treatment.—On November 3, 1941, a double-plane fluoroscopically assisted gastroscopy was undertaken for removal of the tubes. Two rubber drainage tubes, each about eight inches in length were localized in the stomach along the greater curvature and in the cardia. Each of them was grasped at the distal end with

CONGENITAL CYST OF COMMON DUCT

forward-grasping forceps and removed. It was necessary to reinsert the gastroscope following the removal of the foreign body. A 9 mm. x 53 cm. gastroscope was used. He was discharged as well November 4, 1941. His weight at that time was 149 pounds. Because of the interest of his case, he was instructed to return in several months for further study.

On June 6, 1942, a plain roentgenogram of the abdomen was negative. The patient was seen December 7, 1942. He stated that he weighed 155 pounds, had an excellent appetite, and could eat any food without distress. He reported absence of jaundice, and said that his stools and urine were of normal color. His work as a planer in a factory did not cause him to fatigue easily.

For this study 175 cases of congenital cystic dilatation of the common bile duct have been collected from the entire literature. Of this number 82 were taken from the review by Zininger and Cash¹⁴⁸ (1932). The



Anastomosis of both Hepatic Ducts to first portion of Duodenum completed

FIG. 10.—Right and left hepaticoduodenostomy completed over retained catheters. case of Reel and Burrell,⁹⁶ included by these authors, is not included in the present review, since much doubt is cast upon its authenticity by Poate and Wade⁹⁵ (1941) who believe it should be excluded. From the review by the latter authors 23 added cases are taken. From the review of Japanese literature by Yotuyanagi¹⁴⁴ (1936) 42 cases are included. Of this series 6 were previously included by Zininger and Cash,¹⁴⁸ and Poate and Wade,⁹⁵ so that 36 additional cases are not included. Those of Tanaka,¹⁴⁴ Kawaisi¹⁴⁴ (2nd and 3rd cases), Watanabe,¹⁴⁴ Isimaru¹⁴⁴ (3 cases), and Sioda¹⁴⁴ are excluded because of insufficient or inconclusive data. Those of Terada and Yagi,^{121, 144} Kuriyama,¹⁴⁴ Isoda and Kameda,¹⁴⁴ Akamine,¹⁴⁴ and Kawaisi¹⁴⁴ (1st case) are excluded because they seem to represent cases of congenital atresia of the common duct. Two additional cases by Japanese authors and not reported by Yotuyanagi¹⁴⁴ (Murata⁸⁶ and Fujihara⁵⁰) are

included, making a total of 44 Japanese cases. The remaining 34 cases constitute a miscellaneous group in which 14 are taken from reports mentioned in reviews by previous authors, 19 cases not analyzed in previous reviews, and the present case report. The latter 20 cases are analyzed in Table V according to the method of Zininger and Cash¹⁴⁸ (1932) and extended by Poate and Wade⁹⁵ (1941).

The most complete reviews of this subject in the past are those of Waller¹²⁷ (1917), McWhorter⁸¹ (1924), Seneque and Tailhefer¹⁰⁸ (1929), Zininger and Cash¹⁴⁸ (1932), Clark³³³ (1932), Gross⁷⁴ (1933), Yotuyanagi¹⁴⁴ (Japanese literature (1936), Walton¹²⁹ (1939), Poate and Wade⁹⁵ (1941), and Bangerter¹¹ (German, 1941).



FIG 11 — Plain roentgenogram of abdomen showing catheters in place

INCIDENCE

The extreme rarity of this disease is illustrated by the fact that Judd and Greene,⁶³ in 1926, reported only one case of congenital cystic dilatation of the common bile duct in 17,381 operations on the biliary tract. Furthermore, we have been able to collect only 175 cases. Of these, 44 cases, or 25%, are reported by Japanese authors, so that the disease appears to be relatively more frequent in that country.

CONGENITAL CYST OF COMMON DUCT

In Chart 1 the distribution according to sex and age-group is shown. Females accounted for 77% of the cases. The disease occurs predominantly in children and young adults, since 76% of the patients were below 25 years of age.

ETIOLOGY

Many theories have been advanced to explain the etiology of this unusual lesion, and the following represent the views set forth by the various authors:

1. The cystic dilatation is of "congenital origin" and due to malformation of the choledochus (Giezendanner,⁵¹ Heiliger,⁵⁷ Krabbel,⁷⁰ Schürholz,¹⁰⁵ and Seeliger¹⁰⁷).

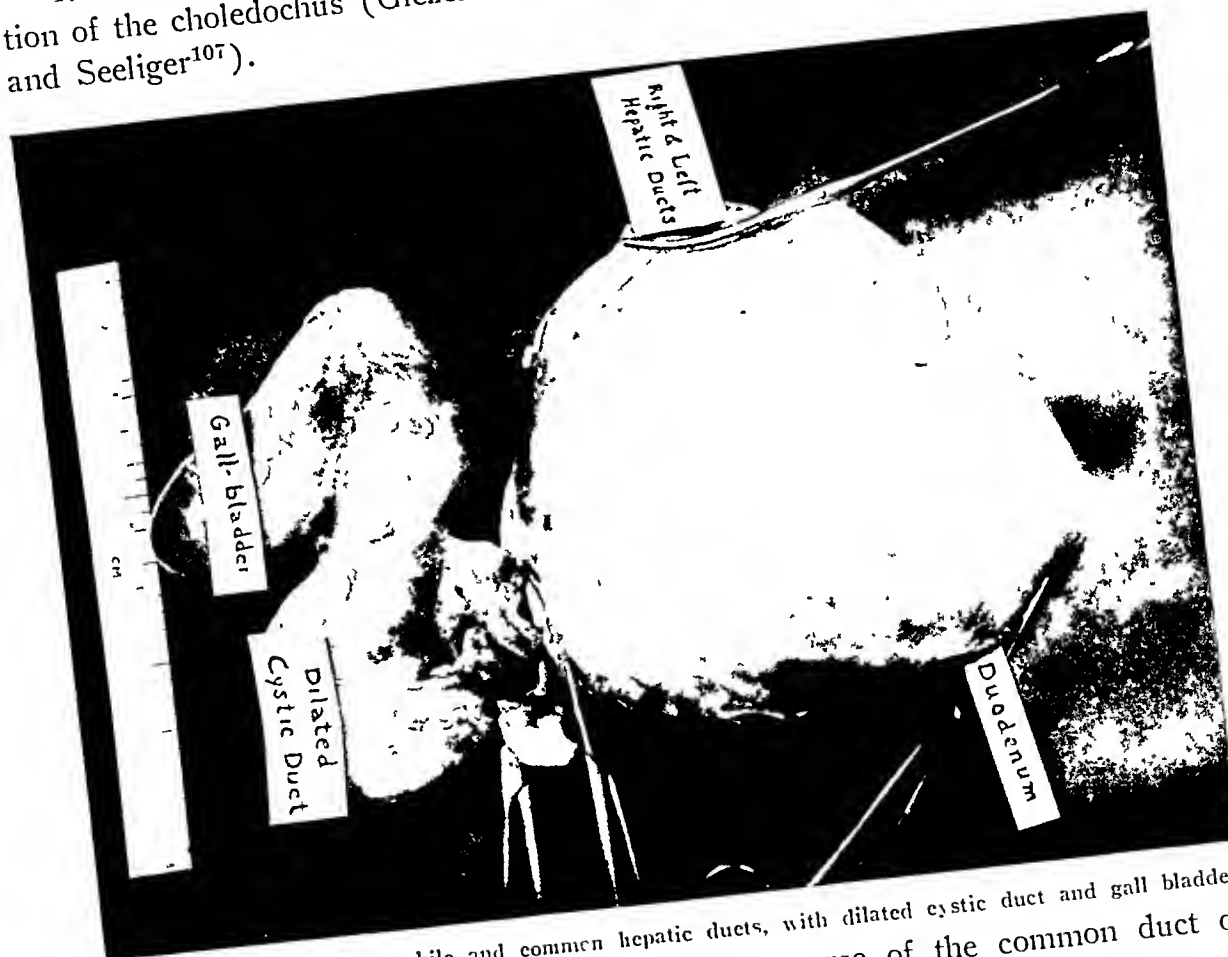


FIG. 12.—Cyst of common bile and common hepatic ducts, with dilated cystic duct and gall bladder.

2. The cyst is caused by an abnormal course of the common duct or angular insertion into the duodenum, congenital in origin, which causes kinking and obstruction (Rostowzew,⁹⁹ Arnolds,⁴ Konitsky,⁶⁸ Ebner,⁴⁰ Russell,¹⁰¹ and Schloessmann¹⁰⁴).

3. The cyst is the result of congenital narrowing of the intraduodenal portion of the choledochus, or stenosis due to infection (Edgeworth⁴¹ and Ladd⁷²).

4. The cyst is caused by a congenital weakness of the wall of the duct (Dreesman,³⁸ Lavenson,⁷⁴ Mayesima,⁷⁹ Neugebauer,⁸⁸ Kolb,⁶⁷ Weiss,¹³³ Bolle,²² Russell,¹⁰¹ and Heiliger⁵⁷). This condition may be similar to congenital idiopathic hydronephrosis in which there may be no demonstrable obstruction (Bohmanson²¹).

5. There is a cystic dilatation on a congenital basis, but with one or more

modifying factors as infection, spasm, kink, valve formation, or stenosis which cause further development of the condition (Zipf¹⁴⁹).

6. Achalazia may be present at the sphincter of Oddi, causing obstruction by neuromuscular incoordination (Rolleston⁹⁷). Weber¹³¹ agrees with this concept, and believes the condition is explainable on the basis of "autonomic neurodysplasia." The similarity in etiology to megalocolon, megaloesophagus, and megaloureter is suggested, and Weber states that the term "megalocholedochus" is applicable.

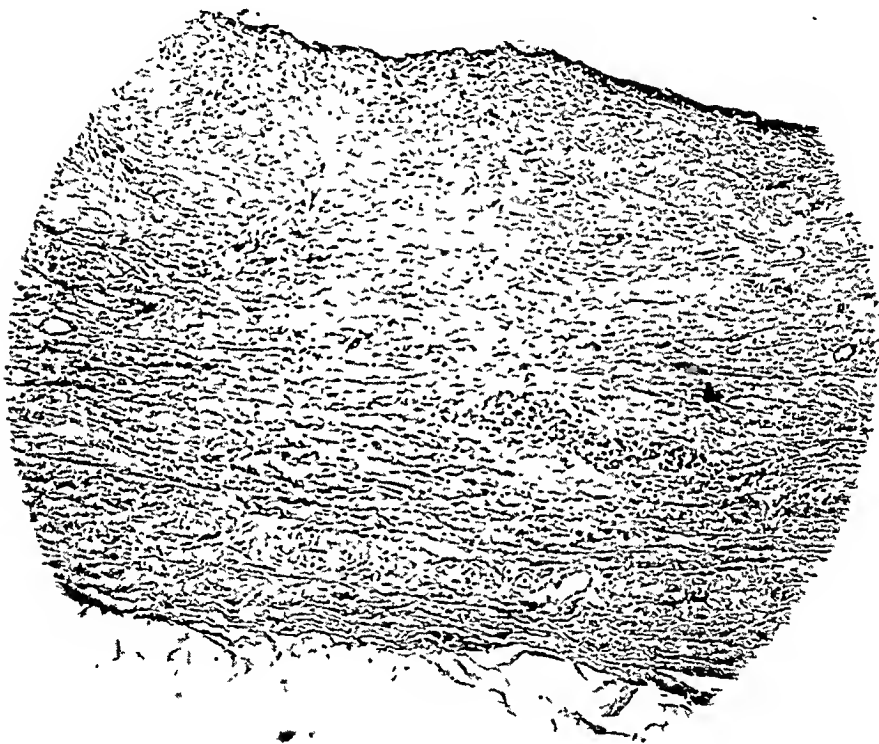


FIG. 13.—Photomicrograph of wall of cyst. (x 100)

7. The cystic dilatation may be caused by the presence of a valve-like fold of tissue over the mouth of the intraduodenal portion of the choledochus (Bakes,¹⁰ Sternberg,¹¹³ Clairmont,³² Neugebauer,⁸⁸ and Rostowzew⁹⁹).

8. Rests of pancreatic tissue in the wall of the choledochus weaken it and permit local dilatation. An analogy is drawn to diverticula of the duodenum in association with aberrant pancreatic tissue (Budde²⁵).

9. The cyst may spring from an abortive diverticulum from the choledochus similar to the diverticulum which gives rise to the ventral pancreas (Winternitz¹³⁸).

10. Choledochus cysts may spring from accessory gallbladder formations which are evaginations from the common duct (Budde²⁵ and Erdely⁴³).

11. The cyst may represent a complication of pregnancy as by pressure

CONGENITAL CYST OF COMMON DUCT

from the enlarging uterus (Goldammer³³), or a kink in the common duct due to the release of intra-abdominal pressure following delivery (McWhorter⁸¹).

12. The cyst may follow abdominal trauma (Kremer⁷¹).

13. The cyst may be caused by pressure on the common duct by enlarged tuberculous mesenteric nodes (Douglas⁷⁷).

14. The dilatation may be caused by narrowing of the duct below by persistence of the fetal physiologic epithelial occlusion (Böhm).²⁰

15. The etiology lies in the inequality of proliferation of the epithelial cells at the stage when the primitive choledochus is still solid, perhaps at the stage of physiologic epithelial occlusion. If there is a more energetic proliferation of the cells of the upper segment during the stage of physiologic

DISTRIBUTION OF CASES ACCORDING TO AGE GROUP AND SEX

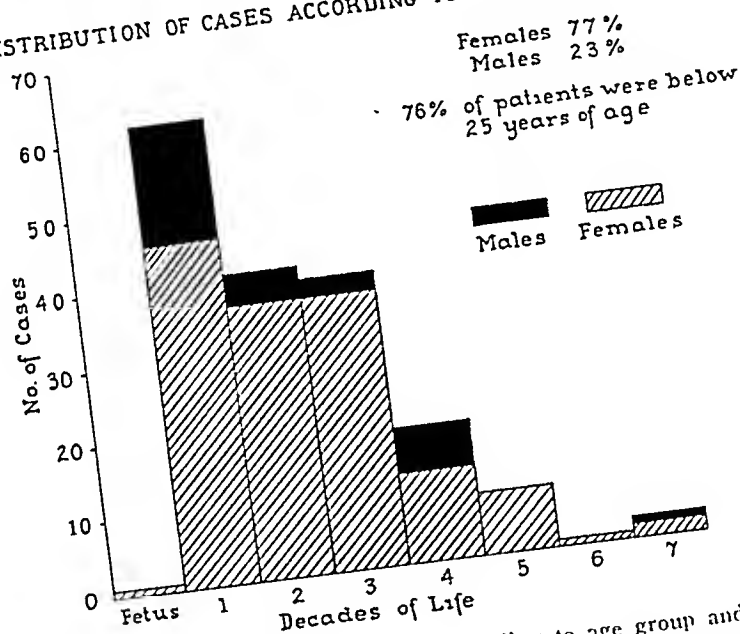


CHART 1.—Distribution of cases according to age group and sex.

epithelial occlusion and less energetic proliferation of the lower segment during the same stage, then, when recanalization occurs later, the upper part of the duct will be abnormally wide and the lower part relatively narrow (Yotuyanagi,¹⁴⁴ 1936).

In consideration of the various theories, it seems most certain that a congenital maldevelopment forms the basis of the abnormality. The theory which appears the most plausible and seems to explain the greatest number of cases is that of Yotuyanagi¹⁴⁴ (1936). His theory is simple, based on sound embryologic principles, and, furthermore, offers a common etiologic basis for the other congenital lesion of the biliary tract with which this lesion is often confused, namely, congenital atresia.

PATHOLOGY

Cystic enlargement of the common bile duct is referred to in the literature as choledochus cyst, cystic dilatation, choledochocoele, diverticulum of the duct, and megalochodochus. It is also referred to as congenital or idiopathic.

The characteristic pathologic change is a cystic dilatation of that portion of the common bile duct lying above the duodenum. The intraduodenal portion and lower two centimeters of the common bile duct are not involved in the dilatation as a rule. The lesion involves the whole circumference, and is thus not a diverticulum. It is not a cyst in the strict sense of the word, but may be termed "cystic" as it has a relatively thin wall and is full of bile. As a rule, only the common bile duct is involved in the cystic dilatation, so that at the upper pole there are two openings—the common hepatic duct and the cystic duct. In some cases, however, as the case being reported, Cases 1, 2, 3, and 6 of Walton,¹²⁹ and in the case of Fowler,⁴⁸ the common hepatic duct shares in the formation of the cyst, thus accounting for three openings at the upper pole—the two hepatic ducts, and the cystic duct. At the lower pole the cystic dilatation communicates with the duodenum by means of the lower uninvolved part of the choledochus.

The pathologic findings in congenital cystic dilatation differ from those found in obstruction of the common bile duct by internal or external pressure. The cyst is spherical but always eccentric and thus differs from the uniform dilatation seen above an obstruction. Furthermore, in the congenital type the enlargement is usually localized, whereas in the common types due to stone, tumor, traumatic stricture, or pancreatitis the extrahepatic and intrahepatic ducts and often the gallbladder enlarged as a whole above the site of obstruction.

The cyst may vary in size from a walnut to a mass larger than a full term pregnancy. The amount of fluid may vary from 30 cc. to several liters. In Yotuyanagi's¹⁴⁴ second case the cyst contained 5,200 cc. and Fukada's¹⁴⁴ first case contained 5,000 cc. In the case of Reel and Burrell,⁹⁶ disputed by Poate and Wade⁹⁵ (1941) as not being an authentic case, 8,000 cc. are reported. There is little relationship between the duration of symptoms and the size of the cyst. In Bolle's case the cyst was "larger than a man's head," and symptoms had been present for only two weeks. In Krabbel's⁷⁰ case the cyst was "the size of a fist," and symptoms had been present for eight years.

The cyst wall is usually thickened, seldom thinned out. It may vary from 2 to 7.5 mm. in thickness. The characteristic histologic picture of the common duct is usually lost, so that only a fibrous sack composed of dense connective tissue remains. Sometimes elastic fibers and smooth muscle elements are present, and rarely glands. The lining of the cyst usually lacks epithelium, but cylindrical or cuboidal epithelium may be present. The inner surface may be roughened and coated with heavy irregular deposits of bile pigments. In infected cases there may be purulent exudate on the inner wall and sometimes ulceration. As a rule the cyst wall shows microscopic evidence of extensive inflammatory reaction.

Some authors have described valve-like folds within the cyst. When these thin flaps of tissue are present, they are adjacent to the openings of the ducts. These valves may be several millimeters thick and 1.5 to 2 cm.

CONGENITAL CYST OF COMMON DUCT

in diameter. These flaps when present are found most commonly near the exit of the cyst, but may be adjacent to the hepatic or cystic duct openings.

The cyst contains bile, the character of which no doubt depends on the amount of obstruction present. The bile is apt to be white if obstruction is nearly complete, due to failure of liver function. On the other hand, it may be thick and viscid if obstruction is incomplete and the concentrating power of the gallbladder is retained. In a minority of cases the fluid is clear, thin, and greenish-yellow. The fluid may be sterile in some cases or contain bacteria in others. Schürholz¹⁰⁵ found streptococci and staphylococci as well as gram-negative cocci and rods, Bolle,²² streptococci, Neugebauer⁸⁸ and Walzel,¹³⁰ typhoid bacilli, Saint,¹⁰² colon and typhoid bacilli, Zininger and Cash,¹⁴⁸ paratyphoid bacilli, and Stoney,¹¹⁴ colon bacilli. In Bangerter's¹¹ first case the contents were sterile, and in the second case there were gram-positive and gram-negative rods. Stones in the cyst are found only exceptionally (cases of McWhorter,⁸¹ Winterstein,¹³⁹ and Sato¹⁴⁴).

The ducts at the upper pole of the cyst are usually greatly dilated, but this dilatation is cylindrical and does not constitute a part of the cyst. This dilatation rarely extends up to the intrahepatic ducts. In contrast to the dilatation of the ducts at the upper pole is the characteristic constriction of the choledochus at the lower pole of the cyst. Great interest and much speculation has centered around this portion of the choledochus, especially with regard to explanation of etiology of the cyst itself and the obstructive symptoms. Although this portion of the duct is usually narrowed, a great variety of conditions may be present. Angulations and kinks are common. Very large cysts may lie immediately against the duodenum in the region of the ampulla of Vater, leaving only a few millimeters of normal duct to join the cyst to the duodenum. If the cyst is in the upper part of the common bile duct, the lower section may be entirely normal. In some of the reported cases (Erdely,⁴³ Weiss,¹³³ Ashby,⁶ Arnolds,⁴ Rolleston,⁹⁷ Giezendanner,⁵¹ and Wyllie¹⁴²) this portion of the duct was obliterated. This obliteration is probably inflammatory in origin, and is sharply to be differentiated from those that are congenital. The age of the patients in these cases precluded the possibility of the obliteration being congenital, and there was a period of months or years in each of these cases during which the patients were free of jaundice. It is probable that congenital stenosis existed with superimposed inflammation and obliteration.

Fowler's⁴⁸ case is a notable exception in that the lower part of the duct was greatly dilated. Wheeler¹³⁵ (1940) reports a peculiar case of a cherry-sized cyst involving only the intraduodenal part of the common bile duct.

As a rule the constriction of the lower part of the choledochus, when it occurs, does not extend down to the ampulla, and the pancreatic duct is unaffected. In the cases of Seeliger¹⁰⁷ and Mayesima⁷⁹ the dilatation occurred so low in the choledochus that the pancreatic duct opened directly into the cyst.

The gallbladder is displaced laterally and is usually of normal size, even

if the cystic duct is dilated. Cases in which the gallbladder is dilated are usually those in older patients in whom the process has been of long duration. In some cases the gallbladder is contracted. Very seldom does it contain stones or gravel. It usually contains clear bile, but in some cases may be empty and chronically inflamed.

The pathologic changes in the liver are not uniformly characteristic and no doubt depend on the degree of obstruction. Frequently the liver is enlarged. Cirrhosis is common, the liver being of a firm consistency and having a fine pebbly surface. The intrahepatic ducts are not dilated as a rule. Microscopically, one finds evidence of cirrhosis with increased periportal connective tissue and proliferation of bile capillaries. Infection is frequent, and the portal areas are markedly infiltrated with leukocytes in these cases. Cholangitis is common and may reach the stage of intraductal suppuration. In advanced cases the presence of lesions characteristic of Banti's syndrome are sometimes found (cirrhosis of the liver and splenomegaly) and may possibly be due to pressure on the portal vein by the cyst and chronic obstruction to flow of bile. In these cases ascites may also be present, and may be due to cirrhosis of the liver or pressure of the cyst on the portal vein. In Walton's¹²⁰ first case there was ascites but no true cirrhosis; the portal, splenic, and superior mesenteric veins were thrombosed.

When the cyst is of sufficient size the gastro-intestinal tract is displaced by its presence. The enlarging cyst lies behind and above the duodenum and spreads upwards to the liver, downwards towards the pelvis, and laterally towards the right renal fossa. The stomach is displaced downwards and to the left, the duodenum downwards, medially, and anteriorly, and the hepatic flexure downward and anteriorly.

Two very unusual pathologic findings are recorded in the literature. The first is that present in the case of Swartley and Weeder¹¹⁷ in which a double common bile duct was present with congenital cystic dilatation confined to the right side. The second is that present in the case of Blocker¹⁸ in which there was traumatic rupture of the cyst following the fall of a 14-year-old boy from a swing across the back of a park seat.

SYMPTOMS AND SIGNS

The salient features of the symptoms and signs of congenital cystic dilatation of the common bile duct constitute a much stressed triad—tumor, jaundice, and pain.

The condition seldom begins suddenly. With careful questioning one can usually trace the onset of symptoms back to early childhood. One may then obtain a history of mild attacks of indigestion with slight upper abdominal discomfort or pain, and mild jaundice which subsided and was given no significance. The longer the interval between these mild attacks, so much the more easily are they forgotten. Until actual obstruction to the bile flow occurs or infection, the condition remains symptomless, and the only sign present is a cystic tumor in the right upper quadrant of the abdomen. In

many cases a typical gallstone history is obtained, with attacks of colicky pain in the right upper abdomen, radiating around the right costal margin and toward the right shoulder, accompanied by nausea and vomiting. The attacks become more frequent, and jaundice, intermittent at first, may become permanent. Often, however, the condition may proceed unnoticed by the patient. Jaundice may become more prominent and unaccompanied by pain. Finally, however, there may arise a feeling of pressure in the liver area, vague discomfort in the epigastrium, anorexia, weakness, hemorrhagic tendencies, and eventually cachexia.

Usually one or two of the triad of diagnostic symptoms and signs are outstanding. Seldom are all three outstandingly present or entirely missing. Table I gives the percentage of these in the present series.

Tumor was present in 77% of the cases, absent in 21%, and questionable or not reported in 2%. In very early cases the tumor may be too small to be palpated definitely, and give only a sense of increased resistance or the suggestion of a mass below the right costal margin and in the right flank.

TABLE I.
THE DIAGNOSTIC TRIAD

	Diagnostic Triad					
	Tumor		Jaundice		Pain	
	Cases	%	Cases	%	Cases	%
Present	134	77	122	70	103	59
Absent	37	21	49	28	61	35
Questionable or not reported	4	2	4	2	11	6

On the other hand, it usually becomes palpable during an attack of pain and jaundice. It may be so large as to fill almost the entire abdomen. It is smooth, elastic, mobile, and may or may not move with respiration. It may be slightly tender. Occasionally on this larger tumor a second smaller mass may be felt—the gallbladder. The liver may be slightly enlarged, but is often not palpable.

Jaundice was present in 70% of the cases, absent in 28%, and questionable or not reported in 2%. The jaundice may be slight, intermittent, or intense and of long-standing. In many cases the stools are acholic, and biliary pigments are present in the urine, these findings varying with the degree of jaundice. The jaundice is of the obstructive type, produced apparently by pressure upon or kinking of the intraduodenal portion of the common bile duct. Thus, the qualitative van den Bergh reaction is usually the positive direct type, and the serum bilirubin is elevated above normal limits, depending on the degree of obstruction. The bromsulfalein test may show liver functional damage by varying degrees of dye retention, and the prothrombin time is often very low, thus accounting for the tendency to hemorrhage reported in the cases.

Pain was present in 59% of the cases, absent in 35%, and questionable or not reported in 6%. This is probably due to increased pressure within

the biliary tree, possibly increased by the presence of infection. Infection is common and probably secondary to stagnation of bile. It is similar to empyema of the gallbladder with cystic duct obstruction. The pain is usually experienced in the epigastrium or right upper quadrant of the abdomen. It is often slight and of a nagging, dragging nature, due to pressure, or discomfort from the abdominal mass. Frank colicky pain may occur and be accompanied by nausea and vomiting. There is no relation between the size of the cyst and the severity of the pain.

Vomiting, when present, usually accompanies the colicky pain or the local peritonitis in infected cases. According to Morley⁸⁴ it may be the consequence of a partial duodenal ileus caused by pressure of the cyst on the root of the mesentery. According to Walton,¹²⁹ vomiting of bile may follow a sudden abundant flow of bile into the duodenum from the cyst.

Fever is absent in the majority of cases but may be present, particularly in cases with infection of the cyst contents or accompanying inflammation of the gallbladder. It may be a manifestation of cholangitis or hepatitis. It is seldom high except in unusual instances.

Signs of acute peritoneal irritation or inflammation denote cases with infection of the cyst contents or an accompanying cholecystitis. Cases with such manifestations were those of Zininger and Cash,¹⁴⁸ Saint,¹⁰² and the second case of Bangerter.¹¹ The cyst was perforated in Walton's¹²⁹ sixth case, and also in the case of Blocker¹⁸ (due to trauma).

At the time the patient is admitted to the hospital the general condition is often poor. The patients usually present themselves with liver damage, anemia, and occasionally ascites due to pressure on the portal vein or cirrhosis of the liver. Albumin and casts may be present in the urine.

Roentgenologic studies may be of great aid in many instances. A plain film of the abdomen usually shows a faint shadow of the cyst, which in unusual cases of calcification of the wall becomes distinctly visible. Cholecystogram rarely shows the gallbladder, since in most cases this organ will not concentrate the dye sufficiently. The case of Wright¹⁴¹ (1935) is the first recorded one in which the gallbladder definitely was visible, showing a peculiar pressure deformity produced by the cyst. However, some of the dye may accumulate in the cyst itself and show an intensification of the shadow shown in the plain film. Gastro-intestinal studies, with barium by mouth and by enema, aid in outlining the positions of neighboring parts of the gastro-intestinal tract. The stomach is displaced to the left and downwards, and may show evidence of external pressure along the lesser curvature. The duodenum is usually displaced medially and anteriorly. It may be somewhat dilated, representing duodenal ileus due to pressure of the cyst on the root of the mesentery. The coils of jejunum may be displaced to the left and downward. The hepatic flexure and transverse colon are displaced downward. The intravenous urogram may be normal, show a tendency to retention of the contrast material in the upper part of the right ureter (as in the present case report), or a slight to moderate degree of hydrone-

phrosis of the right kidney with dilatation of the ureter down to the level of the maximum diameter of the cyst (Wright,¹⁴¹ 1935).

Peritoneoscopy may be undertaken as a diagnostic aid, as shown in the present case report. In experienced hands this procedure is of value and is to be recommended in cases in which the diagnosis is obscure. The danger of puncture or rupture of the cyst on introduction of the instrument should be kept in mind.

DIAGNOSIS

The triad of symptoms and signs—tumor, jaundice, and pain in a child or young adult, especially a female, should make the diagnosis of congenital cystic dilatation of the common bile duct probable. Blood chemistry and urine studies, liver function tests, prothrombin time determinations, roentgenologic studies, and peritoneoscopy should strengthen the diagnosis. It appears that failure of diagnosis is due to the rarity of the condition, and thus the possibility of congenital cystic dilatation of the common bile duct is usually not considered as a cause of the patient's complaints.

TABLE II.
DIAGNOSES MADE IN 175 CASES

Preoperative Diagnosis	No of Cases	Percentage
1 No diagnosis or none stated	59	34
2 Miscellaneous incorrect diagnoses	35	20
3 Choledochus Cyst { First diagnostic impression Mentioned as possible or suspected	15 7	8.6 4.0
4 Echinococcus Cyst	17	9.7
5 Cholecystitis or Cholelithiasis	15	8.6
6 Pancreatic Cyst or Tumor	12	6.9
7 Stone in Common Duct	6	3.4
8 Retroperitoneal Cyst Tumor, or Sarcoma	6	3.4
9 Hydrops or enlarged Gall Bladder	4	2.3
10 Cyst of the Liver	3	1.7
11 Obstructive Jaundice	3	1.7

DIFFERENTIAL DIAGNOSIS

In the present series of 175 cases the diagnosis was correctly made 15 times, or in 8.6%; it was mentioned as a diagnostic possibility 7 times, or in 4% of the cases. In most cases either no diagnosis was made or several incorrect diagnostic possibilities were mentioned. In some of the cases the diagnosis was not made even at operation, and in these the result was usually fatal.

Table II shows the diagnoses most commonly made. Among the miscellaneous incorrect diagnoses not mentioned in the table were congestion of the liver, cirrhosis of the liver, splenic anemia, tumor of the liver, hepatic carcinoma or sarcoma, liver abscess, biliary obstruction, congenital abnormality or obliteration of the biliary tract, empyema of the gallbladder, malignancy of the gallbladder, gastric carcinoma, intestinal occlusion, intussusception,

mesenteric cyst, cyst of the kidney, Wilm's tumor of the kidney, hypernephroma, hydronephrosis, ovarian cyst, ruptured viscus, perforated ulcer, abdominal neoplasm, retroduodenal tumor, generalized tuberculosis, and congenital heart disease.

Echinococcus cyst of the liver presents symptoms and signs similar to those of choledochus cyst. This disease may be differentiated in some cases by experienced physicians by eliciting the so-called "hydatid thrill." There may be eosinophilia and the complement fixation test may be positive. The most satisfactory test is the intradermal Casoni reaction, which is both rapid and specific.

Congenital cysts of the liver are usually small and multiple, often associated with cystic kidneys, and as a rule manifest their presence in adult life.

Pancreatic cysts at the head of the gland may produce pressure on the common bile duct and render differential diagnosis difficult or impossible. A pancreatic cyst usually remains the same size or may progressively increase, whereas a choledochus cyst may enlarge or decrease in size from time to time. Pancreatic cysts may also be found more to the left side than that found in choledochus cyst.

Retroperitoneal neoplasms are usually characterized by rapid progression toward a fatal issue. In cases of jaundice with pain slight or absent, one must rule out carcinoma of the ampulla of Vater or the head of the pancreas. Intermittency or relatively long duration of symptoms should eliminate malignancy as a strong diagnostic possibility.

Congenital atresia of the bile ducts occurs only in infants. Jaundice is progressive from birth, and death occurs within four to six months. Age is thus the decisive factor in differential diagnosis.

If pain and jaundice are prominent, the possibility of biliary stones must be considered. However, one must remember that gallstones are uncommon in childhood, and that choledochus cyst occurs predominately in patients under 25 years of age. Roentgenologic studies will aid in indicating the presence or absence of stones.

TREATMENT AND RESULTS

The various types of treatment used and the respective end-results are summarized in Table III.

I. With absence of surgical treatment the patients eventually die, and in all previous reviews the mortality has been 100%. Death is due to biliary cirrhosis, cholangitis, hemorrhage, or rupture of the cyst. In this series the mortality is quoted as 95%, since one patient (case of Wright,¹⁴¹ 1935) was discharged as unimproved following diagnosis by roentgenology. The only complaint was a mass in the right upper abdominal area, and further information is not available as to her further progress. She was advised to refrain from strenuous exercise. Since in some cases the condition was present for years without causing marked impairment of health, there is no reason to believe that this patient will not eventually fall prey

to obstruction and infection. It is obvious that surgical intervention offers the only hope of cure.

II. Aspiration has no benefit whatever and may lead to peritonitis. The mortality is 100%.

III. Drainage of the cyst, with or without cholecystectomy, is unsatisfactory treatment and carries a high mortality (83% in this series). In Kiselev's⁶⁵ case the fistula closed after one and one-half years. McConnell⁸⁰ reports a case in which the fistula was closed for two months, reopened for eight months, and then closed again. The fistula in Clairmont's³² case remained open, and the patient died three years later of tuberculosis. In Wheeler's¹³⁵ case of cyst of the intraduodenal portion of the common bile duct, the cyst was drained internally by opening the duodenum and incising the cyst. The cases of Sumpter,¹¹⁵ Matida,¹⁴⁴ and Bangerter¹¹ (second case) also recovered.

IV. Drainage followed by secondary anastomosis of the biliary system and gastro-intestinal tract was performed in 24 cases, with a mortality of 29%. In one case, in which recovery ensued, the cyst was excised at the first operation. The disadvantages of this two-stage procedure are the

TABLE III.

TYPES OF TREATMENT IN CASES REPORTED IN THE LITERATURE

Type of Treatment	Cases	Recoveries	Deaths	Mortality
I No surgical treatment	22	1 ^a	21	95 %
II Aspiration	5	0	5	100 %
III Drainage \pm cholecystectomy	40	7	33	83 %
IV Drainage followed by secondary anast. of biliary system & GI tract	24	17	7	29 %
A. Drainage followed by secondary anast. of cyst to G.I. tract	23	16	7	30 %
B. Cyst excised with drainage; secondary anast. to intestine	1	1	0	0 %
V Primary anastomosis of biliary system and G.I. tract	60	44	16	27 %
A. Cyst excised with primary anastomosis of ends of duct	1	1	0	0 %
B. Cyst excised with primary anastomosis of choledochus, common hepatic duct or both hepatic ducts to G.I. tract	7	4	3	43 %
C. Primary anastomosis of cyst and G.I. tract \pm cholecystectomy	47	34	13	28 %
D. Cholecystenterostomy	4	4	0	0 %
E. Primary anastomosis of cyst to stomach, gastro-enterostomy and entero-enterostomy	1	1	0	0 %
VI Miscellaneous	24	3	20	83 %
A. Resection of cyst wall	2	1	1	50 %
B. Excision or attempted excision of cyst \pm drainage	10	1 ^b	9	90 %
C. Cyst excised; secondary cholecysto-enterostomy	1	0	1	100 %
D. Insertion of elastic drainage tube between cyst and duodenum	1	0	1	100 %
E. Fixation of cyst on abdominal wall \pm subsequent aspiration \pm gastro-enterostomy	4	0	4	100 %
F. Laparotomy & aspiration, secondary cholecystoduodenostomy subsequent aspiration & drainage of cyst; subsequent laparotomy & drainage	1	1	0	0 %
G. Nature of operation not known	5 ^c	0	4	80-100 %
(all types) TOTAL	175	72	102	58 %
(surgical operative) TOTAL	148	71	76	51 %

a-This patient was discharged as unimproved following diagnosis by x-ray. (Wright) 1935
The only complaint was a mass in the right upper abdominal area. No information is available as to her further progress.

b-Case of cyst of double common bile duct with cyst of right duct. Cyst was excised.

c-The outcome of one case was not known.

formation of an external biliary fistula, hemorrhagic tendency due to low prothrombin values, and the extra burden of two operations. In cases in which the operative risk is very great, however, as by marked debilitation or presence of infection, drainage for a short time followed by choledochoduodenostomy as a two-stage procedure may be advisable. In order to prevent hemorrhage during the period of drainage, the patient should receive vitamin K and bile salts in adequate quantities by mouth, and the prothrombin time should be kept within normal limits.

V. Primary anastomosis of the biliary system and gastro-intestinal tract is the treatment of choice and is accompanied by the lowest mortality. In the present series the mortality with this procedure was 27% in 60 cases. In most cases the treatment advocated by Bakes,¹⁰ in 1907, was carried out, namely primary anastomosis of the cyst itself to the duodenum. The remaining dilated duct, however, may harbor regurgitated food and infection, and may lead to severe ascending cholangitis (case of Fowler¹⁸). Extirpation of the cyst with primary anastomosis to the duodenum is doubtlessly the most physiologic procedure, for it creates a new anatomic union between the liver and duodenum and removes the cyst which harbors infection. This method, however, carries a higher mortality and is advocated therefore only in cases in which the patient is a good operative risk, the cyst large, and preferably in the absence of infection. In cases in which there is free communication between the gallbladder and the cyst, anastomosis of this organ to the small intestine has given excellent results. This was carried out in four cases, with recovery in each.

VI. A review of the miscellaneous procedures used in treatment reveals a mortality of 83%. In most of these cases the true pathologic condition was not recognized even at operation, and thus a proper rationale for the surgical procedure is lacking.

In cases surgically treated the most common causes of death were shock, hemorrhage, asthenia and debilitation, cholangitis, and peritonitis.

In short, the preferred surgical treatment is to anastomose the cyst to the duodenum, or better, if possible, to excise the dilated part of the common duct and anastomose the remainder to the duodenum. The former is a simpler procedure, carries a lower mortality, and is best undertaken when the operative risk is great. In all cases the prothrombin time should be carefully checked preoperatively and brought to as near normal level as possible by the use of vitamin K and bile salts.

PROGNOSIS

A review of the early literature would give a very gloomy outlook as to prognosis. Each subsequent review of the literature, however, reveals a higher percentage of recovery following operation. In 1927, Lange⁷³ reported 53 cases in which only 9 had recovered following operation (mortality of 83%). Tailhefer^{108, 118} found 29 recoveries out of a series of 82 cases in 1929 (mortality of 65%) as opposed to 49 recoveries out of a series of 115

CONGENITAL CYST OF COMMON DUCT

cases in 1934 (mortality of 57%). The present series shows 71 recoveries out of a total of 148 operated cases (mortality of 51%). Walton,¹²⁹ in 1939, reported four cases of recovery out of his five cases operated upon.

The factors involved in prognosis are the preoperative recognition of the lesion, the condition of the patient at the time of operation, and the type of therapy instituted. Table IV shows the effect of correct preoperative diagnosis on mortality. Thus, in cases in which the diagnosis was correct or suspected the mortality was 36%, whereas in cases in which the diagnosis was incorrect, or none made, the mortality was 62%. Cases seen late are usually poor surgical risks as a result of liver damage, cachexia, and myocardial degeneration due to prolonged jaundice. Early cases give the best prognosis because the patient's condition will usually permit the proper surgical procedure to be carried out in one stage, and postoperative complications are less frequent. The type of surgical treatment is of the greatest importance, and it has been found that primary anastomosis of the biliary system and gastro-intestinal tract carries the lowest mortality and offers the greatest chance of cure.

TABLE IV.

EFFECT OF CORRECT PREOPERATIVE DIAGNOSIS ON MORTALITY				
Preoperative Diagnosis	Cases	Recovered	Died	Mortality
Correct or suspected	22	14	8	36%
Incorrect or none made	153 ^a	57	95	62%

^a-The outcome in one case was not known.

Not a great deal is known about the late results in cases of recovery following operation, since in most cases nothing further is reported concerning the progress of the patient. Cases reported as well after four years are those of McConnell,⁸⁰ Berkley,¹⁵ and Gross⁵⁴ (one case). The following authors report cases in which the patient remained well for more than five years: Iselin,⁶¹ Hildebrand,⁵⁸ McWhorter,⁸¹ Murata,⁸⁶ Walton¹²⁹ (second case), Wheeler,¹³⁵ and Sumpter.¹¹⁵ The case of McWhorter⁸¹ survived for 13 years and died of uremia with nephrosclerosis, hypertension, and diabetes. The case of Wheeler¹³⁵ died 15 years later, at the age of 80, of a medical ailment.

SUMMARY AND CONCLUSIONS

One hundred and seventy-five cases of congenital cystic dilatation of the common bile duct are reviewed. A case report is included. The disease predominates in females and occurs principally in children and young adults.

A congenital maldevelopment probably forms the basis of the abnormality. The most plausible explanation is that of Yotuyanagi¹⁴⁴ (1936), according to whom the etiology lies in the inequality of proliferation of the epithelial cells at the stage of fetal physiologic epithelial occlusion of the common bile duct.

TABLE V

CASES NOT ANALYZED IN PREVIOUS REVIEWS

No.	Author	Year	Sex	Age	Tumor	Jaundice	Pain	Preop. Diag.	Treatment	Results
156	Arullani	1936	F.	34	-	+	-	-	1. Drainage of choledochus. 2. Secondary choledochogastrostomy. Choledochogastrostomy.	Recovery
157	Bangerter	1941	F.	22	-	+	+	Obstructive jaundice. Hemorrhagic diathesis.	Choledochogastrostomy.	Death on 3rd postoperative day.
158	Bangerter	1941	F.	60	-	+	+	Empyema of the gallbladder. Pericholecystic abscess?	Cholecystectomy and T-tube drainage of the cyst.	Recovery.
159	Bodley	1937	F.	2	+	+	-	Retroperitoneal sarcoma.	1. Choledochotomy and choledochoduodenostomy. 2. 25 days later separation of previous anastomosis and performance of choledochoduodenostomy.	1. Improvement for 10 days, then recurrence of symptoms. 2. Death on 2nd postoperative day.
160	Bull	1939	F.	42	+	-	+	Retroperitoneal cyst.	1. Celiotomy and aspiration. 2. Cholecystoduodenostomy 3 wks. later. 3. Aspiration and drainage of cyst 3 weeks later. 4. Celiotomy and further drainage.	Recovery.
161	Carr	1940	F.	4	+	+	+	Probable pancreatic tumor or mesenteric cyst. Possible cystic dilatation of common bile duct.	Choledochoduodenostomy.	Recovery.
162	Duff	1934	F.	62	+	-	+	Retroperitoneal cyst. Possible cyst of common bile duct.	Choledochojejunostomy.	Recovery.
163	Fujihara	1935	F.	13	+	+	-	-	Choledochojejunostomy.	Recovery.
164	Kiselev	1932	F.	33	-	+	+	-	Resection of the cyst wall.	Recovery.
165	Kiselev	1932	M.	15	+	+	+	-	External drainage.	Recovery. Fistula closed after 1½ years.
166	Koch	1936	?	1½	+	-	+	Congenital heart disease.	None.	Died of congenital heart disease.
167	Mendillo and Koufman	1942	F.	1	+	-	-	Wilm's tumor of right kidney.	1. Irradiation. 2. Excision and choledochoduodenostomy. 3. Omentopexy for cirrhosis of the liver.	1. Fever, anorexia, wt. loss, diarrhea. 2. Recovery. 3. Recovery. Pt. alive in Feb., 1941.
168	Masson and Rieniets	1931	F.	8	+	-	-	Mesenteric or hepatic cyst.	Excision of cyst and hepaticogastrostomy.	Death on 2nd postoperative day.

CONGENITAL CYST OF COMMON DUCT

169	Murata	1935	F.	1½	+	-	-	Idiopathic dila- tation of common duct.	Choledoch- duodenostomy.	Recovery. Well after 5 years.
170	Tailhefer	1934	F.	23	+	?	?	-	Choledoch- duodenostomy.	Recovery.
171	Tailhefer	1934	F.	24	+	+	+	Congenital dila- tation of common duct.	Choledoch- duodenostomy.	Death on 4th postoperative day.
172	Wheeler	1915 and 1940	M.	65	-	+	+	Biliary obstruc- tion.	Drainage (duo- denum opened and cyst incised).	Recovery. Died 15 yrs. later of a medical ailment.
173	Winterstein	1932	F.	64	+	+	+	Calculous chole- cystitis.	Cholecystectomy and choledoch- duodenostomy.	Recovery.
174	Wright	1935	F.	39	+	-	-	Congenital cys- tic dilatation of common bile duct.	None. Patient to refrain from strenuous exer- cise.	Patient dis- charged as im- proved.
175	Authors' case	1942	M.	20	+	+	+	Retroperitoneal tumor, probably choledochus cyst.	Extirpation of cyst and gall- bladder. Primary right and left hepaticoduoden- ostomy.	Recovery.

The characteristic pathologic finding is a large cystic dilatation of the common bile duct. The ducts at the upper pole of the cyst are usually dilated, whereas at the lower pole the intraduodenal portion of the duct is usually constricted or angulated. Frequently the liver is enlarged or may show biliary cirrhosis.

The salient symptoms and signs form a diagnostic triad—tumor, jaundice, and pain. Acholic stools may occur, and bile may be present in the urine. The symptoms may begin early in life and occur intermittently over a period of years. Roentgenologic studies and peritoneoscopy may be of aid in confirming the diagnosis. The diagnosis was made or suspected in only 22 cases (12.6%), but consideration of the condition as a diagnostic possibility should lead to more frequent correct diagnosis.

The procedure of choice in treatment is a primary anastomosis of the biliary and intestinal tracts. Anastomosis of the cyst itself to the duodenum is accompanied by the lowest mortality, but in good-risk patients extirpation of the cyst was primary anastomosis to the duodenum is preferable because the cyst may harbor infection and regurgitated food. The latter procedure was performed, with recovery, in the case herein reported.

The mortality in the entire series was 58%, but in those patients treated by primary anastomosis of the biliary and intestinal tracts the mortality was 27%. The prognosis depends on the preoperative recognition of the lesion, the condition of the patient at the time of operation, and the type of therapy instituted.

BIBLIOGRAPHY

- 1 Abe, S.: Three Autopsy Reports. Tr. Soc. path. jap., 25, 423-429, 1935. (In Japanese).
- 2 Adam, L.: Zentralblatt für Chirurgie, 1, 997, 1923.

- ³ Ahrens: Zentralblatt für Chirurgie, **1**, 672, 1920.
- ⁴ Arnolds: Manneskopfgrossen Retentionscyste des Choledochus. Deutsche med. Wchnschr., **32**, 1804, November 1, 1906.
- ⁵ Arullani, C.: La dilatazione idiopatica del coledoco. Boll. Accad. lancia. Roma, **8**, 643-650, 1936.
- ⁶ Ashby, H.: Medical Chronicle, **10**, 28, 1898.
- ⁷ Bachkieroff: Sur la pathogenie des kystes du choledoque. Chir. Arch. Veliaminova, **27**, 63, 1911.
- ⁸ Backer-Grondahl, N.: Idiopathic Cysts of Common Duct. Med. rev. Bergen, **50**, 337-354, August, 1933.
- ⁹ Badile: Archivio italiano di chirurgia, **51**, 424, 1924.
- ¹⁰ Bakes: Wien. klin. Wchnschr., **20**, 298, 1907.
- ¹¹ Bangerter, J.: So-called Idiopathic Cysts. Schweiz. med. Wchnschr., **71**, 677, May 31, 1941; *idem*, *ibid*: **71**, 733, June 14, 1941.
- ¹² Beaufays: Z. org. Chir., **57**, 412, 1932.
- ¹³ Bencevic: Z. org. Chir., **43**, 421, 1928.
- ¹⁴ Bengolea, A. J., and Suarez, C. V.: Idiopathic Cystic Dilatation of Hepatocholedochus; Case. Nord. med. (Norsk mag. f. laegevi dansk), **1**, 31-36, January 7, 1939.
- ¹⁵ Berkley, H. K.: Idiopathic Dilatation of the Common Bile Duct in Childhood. Jour. of Pediatrics, **14**, 79, 1939.
- ¹⁶ Berman, J. K., and Ballenger, F.: Congenital Cyst of Common Duct. Quart. Bull. Indiana Univ. M. Center, **3**, 141-144, October, 1941.
- ¹⁷ Bistrov, P. B.: Kharkovskiv Med. Jour., **19**, 319, 1915.
- ¹⁸ Blocker, T. G. and others: Traumatic Rupture of Congenital Cyst of Choledochus, Arch. Surg., **34**, 695, 1937.
- ¹⁹ Bodley, J. W.: Choledochus Cyst; Case; South, Surgeon, **6**, 126-130, April, 1937.
- ²⁰ Böhm, F.: Ztschr. f. ang. Anat. u. s. w. (Berlin), **1**, 105, 1913.
- ²¹ Bohmanson, C.: Cyst of the Common Bile Duct. Acta Chirurgica Scandinavica, **56**, 440, 1924.
- ²² Bolle, H.: Ein Fall von idiopathischer Choledochuszyste. Deutsche med. Wchnschr., **48**, 1381, October 13, 1922.
- ²³ Broca: Bull. et mem. Soc. nat. de chir., **23**, 209, 1897.
- ²⁴ Brun and Hartman: Bull. et mem. Soc. nat. de chir., **23**, 207, 1897.
- ²⁵ Budde, M.: Über die Pathogenese und das Krankheitsbild der cystischen Gallergangerweiterung (sogenannte idiopathische Choledochuscyste). Deutsche Ztschr. f. chir., **157**, 364, 1920.
- ²⁶ Bull, P.: Idiopathic Dilatation of Choledochus (Congenital Cyst); Case. Nord. med. (Norsk mag. f. laegevi dansk), **1**, 31-36, January 7, 1939.
- ²⁷ Burman, G. E. L.: A Case of Simple Obstructive Jaundice with Huge Dilatation of the Common Bile Duct. The Practitioner, Page 473, March, 1912.
- ²⁸ Butters: Choledochus-Zysten. Deutsche med. Wchnschr., **36**, 1351, July 14, 1910.
- ²⁹ Carr, G. L.: Congenital Cystic Dilatation of Common Bile Duct. M. Woman's J., **47**, 301-303, October, 1940.
- ³⁰ Chiray, M., Albot, G., and Jame, R.: Obstructive Jaundice due to Stenosis of Vater's Ampulla and Cystic Dilatation of Bile Duct in a Girl Seven Years Old. Gaz. med. de France (suppl. Gastro-enterol.), Pages 3-6, November 15, 1933.
- ³¹ Choyce: Cited by Stoney.¹¹⁴
- ³² Clairmont: Zystische Dilatation des Ductus Choledochus. Wien klin. Wchnschr., **24**, 1616, 1911.
- ³³ Clark, J. H.: So-called Idiopathic Choledochus Cyst; Pathogenesis and Pathology; Report of Case with Review of Literature. Internat. Clin. **1**, 78-103, March, 1932.
- ³⁴ De Quervain: Spezielle chirurgische Diagnostik, Page 398, 1922.
- ³⁵ Derwischen: Zentralblatt für Chirurgie, **54**, 852, April 12, 1927.

- 36 Di Natale, L.: Cisti del coledoco, *Arch. ital. di chir.*, 23, 553, May, 1929; abstr. *Brit. M. J.*, 2, 30, August 24, 1929.
- 37 Douglas: *Monthly J. M. Sc. (London)*, 14, 97, 1852; cited by McWhorter,⁸¹ and Dreesman.³⁸
- 38 Dreesman: Beitrag zur Kenntnis der kongenitalen Anomalien der Gallenwege. *Deutsche Ztschr. f. Chir.*, 92, 401, 1908.
- 39 Duff, D. D.: Cyst of the Common Bile Duct. *Brit. Jour. Surg.*, 21, 536, 1933-34.
- 40 Ebner, A.: Idiopathische Choledochuscyste und Purpura Hemorrhagica Fulminans. *Beitr. Z. klin. Chir.*, 64, 473, 1909.
- 41 Edgeworth, F. H.: A Case of Dilatation of the Common Bile Duct Simulating Distention of the Gallbladder. *Lancet*, 1, 1180, May 11, 1895.
- 42 Elischer: *Zentralblatt für Chirurgie*, 9, 341, 1923.
- 43 Erdely: *Deutsche Zeitschrift für Chirurgie*, 209, 65, 1928.
- 44 Ewoyan: Cited by Sebek.¹⁰⁶
- 45 Exner, A.: Choledochus Cyst. *Wiener klinische Wochenschrift*, 24, 1615, 1911.
- 46 Feyrter, F.: Über Fehlbildungen der extrahepatelen Gallenwege mit Störung der normalen Hohlraumbildung (Verödung, Enge und cystische Erweiterung) und des normalen Gangverlaufes. *Virchows Arch. f. path. Anat.*, 271, 20, 1929.
- 47 Flechtenmacher, C.: Operativ entfernte Choledochuszyste im Ligamentum hepato-duodenale. *Wien. klin. Wchnschr.*, 32, 365, 1919.
- 48 Fowler, R. S.: Choledochus Cyst. *ANNALS OF SURGERY*, 64, 546, 1916.
- 49 Frizelle, E. R.: Idiopathic Congenital Dilatation of the Common Bile Duct. *Brit. Med. Jour.*, 1, 610, 1932.
- 50 Fujihara: *Arch. jap. Chir. (Kyoto)*, 12, 1206-1212, 1935; abstr. in *Z. org. Chir.*, 75, 117-118, 1936.
- 51 Giezendanner, E.: Beitrag zum Studium der kongenitalen Choledochusystem. *Frankfort. Ztschr. f. Path.*, 38, 150, 1929.
- 52 Gokhman, A. I.: Idiopathic Cyst of Common Bile Duct; Case. *Novy khir. Arkhiv.*, 37, 486-489, 1936.
- 53 Goldammer: Beiträge zur Chirurgie der Gallenwege. *Beitr. z. klin. Chir.*, 55, 214, 1907.
- 54 Gross, R. E.: Idiopathic Dilatation of the Common Bile Duct in Children. *Jour. Ped.*, 3, 730, 1933.
- 55 Hamilton, I.: Congenital Cystic Dilatation of the Common Bile Duct. *Med. Jour. of Australia*, Page 800, May 27, 1939.
- 56 Heid: Inaugural Dissertation. Cited by McWhorter.⁸¹
- 57 Heiliger: Inaugural Dissertation. Cited by McWhorter.⁸¹
- 58 Hildebrand: Geheilte Choledochuszyste. *Deutsche med. Wchnschr.*, 39, 2224, November 6, 1913.
- 59 Hill, N. H., and Ramsay, R. A.: Cystic Dilatation of the Common Bile Duct. *Brit. M. J.*, 2, 991, November 28, 1925.
- 60 Ipsen, J.: Et tilfaelde af choledochuscyste. *Hospitalstid*, 45, 1342, 1913. Cited by Waller.¹²⁷
- 61 Iselin, H.: Gemeinsame Cyste der Gallen-und Pankreaswege. *Arch. f. klin. Chir.*, 145, 304, 1927.
- 62 Jauregui, P.: Cyst of the Common Bile Duct. *Rev. de cir.*, 7, 536, 1928.
- 63 Judd, E. S., and Greene, E. L.: Choledochus Cyst. *Surg. Gynec. and Obst.*, 46, 317, 1928.
- 64 Keyrovsky: Inaugural Dissertation. Greifswald, 1888 (in Seyffert¹⁰⁹).
- 65 Kiselev, N.: Idiopathic Dilatation of the Common Bile Duct. *Vestn. Chir.*, 78/79, 182-186, 1932.
- 66 Koch, F.: So-called Choledochus Cyst (Idiopathic Congenital Dilatation). *Hygeia* 98, 577-587, September 15, 1936.

- ⁶⁷ Kolb: Inaugural Dissertation. Cited by Waller¹²⁷ and McWhorter.⁸¹
- ⁶⁸ Konitsky: Inaugural Dissertation; cited by Waller; cited by McWhorter.
- ⁶⁹ Körte: Die Erkrankungen der Gallenwege. *Med. Praxis*, Page 117, 1928. Cited by Seneque and Taillhefer.¹⁰⁸
- ⁷⁰ Krabbel, M.: Zum operativen Heilung der idiopathischen Choledochuscyste. *Beitr. z. klin. Chir.*, 130, 159, 1924.
- ⁷¹ Kremer, J.: Ein Fall einer durch Choledochoduodenostomie dauernd geheilten echten Choledochuszyste. *Arch. f. klin. Chir.*, 113, 99, 1919.
- ⁷² Ladd: *J. A. M. A.*, 91, 1082, 1928.
- ⁷³ Lange, K.: Beitrag zur idiopathischen Choledochuscyste. *Zentralbl. f. Chir.*, 54, 2287, 1927.
- ⁷⁴ Lavenson, R. S.: Cysts of the Common Bile Duct. *Am. J. M. Sc.*, 137, 563, 1909.
- ⁷⁵ Letulle, M.: Dilatation kystique des voies biliaires cholangiectasies congenitales. *Presse med.*, 21, 97, February 1, 1913.
- ⁷⁶ Limito, C.: Idiopathic Cyst of Choledochus; Case. *Arch. ital. di anat. e. isto., pat.*, 6, 619-627, Sept.-Oct., 1935.
- ⁷⁷ Masson, J. C., and Rieniets, J. H.: Adenocarcinoma and Squamous Cell Carcinoma in a Cyst of the Mesosigmoid (Case Report); Choledochus Cyst (Case Report). *S. Clin. North America*, 11, 743-751, August, 1931.
- ⁷⁸ Matthieu, J.: Congenital Cyst of the Common Bile Duct. *ANNALS OF SURGERY*, 92, 159, 1930.
- ⁷⁹ Mayesima, J.: Zur Kasuistik der Primären cystischen Erweiterung des Ductus Choledochus. *Deutsche Ztschr. f. Chir.*, 119, 338, 1912.
- ⁸⁰ McConnell, A.: Cyst of the Common Bile Duct. *Brit. J. Surg.*, 7, 520, April, 1920.
- ⁸¹ McWhorter, G. L.: Congenital Cystic Dilatation of the Common Bile Duct. *Arch. Surg.*, 8, 604, March, 1924.
- ⁸² Melichoff: Dilatation idiopathique du choledoque. *Russkaya klinika*, 3, 74, 1925.
- ⁸³ Mendillo, A. J., and Koufman, W. B.: Choledochus Cyst; Case. *Connecticut M. J.*, 6, 99-101, February, 1942.
- ⁸⁴ Morley, J.: Congenital Cyst of the Common Bile Duct. *Brit. Jour. of Surg.*, 10, 413, 1923.
- ⁸⁵ Morrin: cited by Stoney.
- ⁸⁶ Murata: Über einen dauernd geheilten Fall von idiopathischer Choledochuserweiterung. *Zbl. f. Chir.*, 62, 1269-1271, 1935.
- ⁸⁷ Narabayashi: *Z. org. Chir.*, 25, 401, 1924.
- ⁸⁸ Neugebauer, F.: Zur Kenntnis der idiopathischen Choledochuscyste. *Beitr. z. klin. Chir.*, 131, 448, 1924.
- ⁸⁹ Nicolaysen, J.: *Zentralbl. f. Chir.*, 16, 1269, 1899.
- ⁹⁰ Oglobin, A. A.: Idiopathic Cysts of the Bile Ducts. *Vestnik khir.*, 9, 177, 1927; abstr. *Internat. Abstract Surg.*, Page 324, October, 1928.
- ⁹¹ O'Gorman, F. M., *et al.*: Idiopathic Choledochus Cyst; Report of a Case, *New York State Jour. of Med.*, 31, 1196, 1931.
- ⁹² Olivecrona, H.: Infected Cyst of the Common Bile Duct; Operation; Recovery. *Acta chir. Scandinav.*, 62, 347, 1927.
- ⁹³ Oxley, M. G. B.: Congenital Atresia of the Duodenal Opening of the Common Bile Duct in an Infant, Producing a Large Abdominal Tumor. *Lancet*, 2, 988, December 8, 1883.
- ⁹⁴ Pamperl, R.: *Medizinische Klinik*, 21, 1608, 1925.
- ⁹⁵ Poate, H. R. G., and Wade: Congenital Cystic Dilatation of the Common Bile Duct. *Australian and New Zealand J. Surg.*, 11, 32-45, July, 1941.
- ⁹⁶ Reel, P. J., and Burrell, N. E.: Cystic Dilatation of the Common Bile Duct. *ANNALS OF SURGERY*, 75, 191, 1922.

- ⁹⁷ Rolleston, H. D.: Diseases of the Liver, Gallbladder and Bile Ducts. ed. 3, New York, The Macmillan Co., 1905, p. 651.
- ⁹⁸ Rosenberg: Archives für klinische Chirurgie, 125, 1-2, July 31, 1923.
- ⁹⁹ Rostowzew, M. J.: Ein Fall von hochgradiger cystischer Erweiterung des Ductus Choledochus. Deutsche med. Wchnschr., 28, 739, October 9, 1902.
- ¹⁰⁰ Rotgans: cited by McWhorter.
- ¹⁰¹ Russell, R. H.: Case of Cystic Dilatation of the Common Bile Duct in a Child. ANNALS OF SURGERY, 26, 692, 1897.
- ¹⁰² Saint, J. H.: Cystic Dilatation of the Common Bile Duct. Brit. Med. Jour., p. 230, 1932.
- ¹⁰³ Santrucek, K.: Idiopathic Cyst of Bile Duct. Casop. lek. cesk., 71, 1185-1186, September 16, 1932.
- ¹⁰⁴ Schloessmann: Beitrag zur Kenntnis der Choledochuscysten. Deutsche Ztschr. f. Chir., 109, 160, 1911.
- ¹⁰⁵ Schürholz: Ein Fall von sogenannten idiopathischer Choledochuscyste. Arch. f. klin. Chir., 118, 91, 1921.
- ¹⁰⁶ Sebek: O pricinach ysiniku, pathologii a sympotomologii tak zvane idiopathicke cysty choledochu. Casop. lek. cesk., 66, 1720, 1927. Cited by Seneque and Tailhefer.
- ¹⁰⁷ Seeliger, S.: Beitrag zur Kenntnis der echten Choledochuscysten. Beitr. z. klin. Chir., 99, 158, 1916.
- ¹⁰⁸ Seneque, J., and Tailhefer, A.: Les dilatations congenitales due choledoque. J. de chir., 33, 154, 1929.
- ¹⁰⁹ Seyffert. Cited by McWhorter.
- ¹¹⁰ Sieber, F.: Large Cyst of the Bile Ducts. Zentralbl. f. Gynäk., 53, 2848, 1929.
- ¹¹¹ Smit: Medicinisk Revue, 32, 285, 1915.
- ¹¹² Söderlund: A Case of Stone in the Bile Ducts. Acta chir. Scandinav., 59, 253, 1925.
- ¹¹³ Sternberg, C.: Cholezystostomie. Wien. klin. Wchnschr., 24, 1616, 1911.
- ¹¹⁴ Stoney, R. A.: Cyst of the Common Bile Duct. Irish J. M. Sc., page 764, December, 1929.
- ¹¹⁵ Sumpter, W. D.: South. Pract., 39, 169, 1917.
- ¹¹⁶ Swain, W. P.: A Case of Cholecystenterostomy with the Use of Murphy's Button. Lancet, 1, 743, March 23, 1895.
- ¹¹⁷ Swartley, W. B., and Weeder, S. D.: Choledochus Cyst with a Double Common Bile Duct. ANNALS OF SURGERY, 101, 912, 1935; see further report on the same case by Weeder.
- ¹¹⁸ Tailhefer, A.: Dilatation Congenitale du canal choledoque. Bull. Soc. nat. Chir. Paris, 60, 8-11, 1934.
- ¹¹⁹ Tavernier, M.: Dilatation congenitale du choledoque. Lyon Chir., 31, 595-597, 1934.
- ¹²⁰ Taylor, J.: Cystic Dilatation of the Common Bile Duct: Record of an Example. Brit. J. Surg., 16, 327, 1928.
- ¹²¹ Terrada and Yagi: Jour. of Ped., Tokyo, 317, 2078, 1930; reviewed in Am. Jour. Dis. of Child., 42, 1256, 1931.
- ¹²² Ugelli, L.: Sulle dilatazioni congenite del coledoca: Policlinico (sez. chir.), 40, 343-355, 1933.
- ¹²³ Upcott, H.: Cystic Dilatation of the Common Bile Duct. Brit. Med. Jour., Page 911, 1932.
- ¹²⁴ Vara-Lopez, R., and Meana Negrete, V.: Congenital Cystic Dilatation of Choledochus: Report of Cases. Med. espan., 3, 471-483, June, 1940.
- ¹²⁵ Virgillo, F.: Congenital Cystic Dilatation of Choledochus; Case, Arch. ital. di chir., 54, 873-878, 1938.
- ¹²⁶ Wagner, A.: Beitrag zur Chirurgie der Gallenwege. Deutsche Ztschr. f. Chir., 145, 15, 1918.
- ¹²⁷ Waller, E.: Idiopathic Choledochus Cyst. ANNALS OF SURGERY, 66, 446, 1917.

- ¹²⁸ Walters and Snell: Diseases of the Gallbladder and Bile Ducts. Saunders Co., 1940. Pages 236-240.
- ¹²⁹ Walton, J.: Congenital Diverticulum of the Common Bile Duct. Brit. Jour. of Surg., 27, 295, October, 1939.
- ¹³⁰ Walzel, P.: Zentralblatt für Chirurgie, 48, 594, 1921.
- ¹³¹ Weber, F. P.: Cystic Dilatation of the Common Bile Duct. Brit. Jour. of Child. Dis., 31, 27 and 113, 1934.
- ¹³² Weeder, S. D.: Choledochus Cyst with Double Common Duct; Sequelae and Complications. ANNALS OF SURGERY, 110, 55-59, September, 1939.
- ¹³³ Weiss, S.: Ein seltener Fall von cystischen Erweiterung des Ductus Choledochus. Berl. klin. Wchnschr., 46, 1843, 1909.
- ¹³⁴ Wettwer: Ein Fall von congenitalen Choledochuscyste: Dissertation, Göttinger, 1907; cited by Waller.
- ¹³⁵ Wheeler, W. I. de C.: Dublin Jour. Med. Sci., December, 1915; Unusual Case of Obstruction to Common Duct (Choledochocoele?). Brit. J. Surg., 27, 446-448, January, 1940.
- ¹³⁶ Willis, B. C.: Congenital Cystic Dilatation of the Common Bile Duct. ANNALS OF SURGERY, 87, 48, 1928.
- ¹³⁷ Wilson, H. V., Jr.: Choledochus Cyst. J. A. M. A., 95, 399, August 9, 1930.
- ¹³⁸ Winternitz; quoted by Erdely.⁴³
- ¹³⁹ Winterstein, O.: Bile Duct Cysts: Diagnosis. Wien, med. Wchnschr., 82, 638-639, May 21, 1932.
- ¹⁴⁰ Wright, H. W. S.: Congenital Diverticulum of the Common Bile Duct. Surg., Gynec., and Obst., 39, 156, 1924.
- ¹⁴¹ Wright, A. D.: X-ray Appearances Produced by Congenital Cystic Dilatation of Common Duct. Brit. J. Radiol., 8, 227-230, April, 1935.
- ¹⁴² Wyllie, W. G.: Congenital Cyst of the Common Bile Duct. Lancet, 1, 1342, 1925.
- ¹⁴³ Yamanouchi, K.: Über die cystische Dilatation des Ductus choledochus. Ztschr. f. Jap. Chir. Gesellschr., 22, 1921; abstr., Zentralorg. f. d. ges. Chir., 16, 228, 1922. Cited by Neugebauer, Judd and Greene, and Willis.
- ¹⁴⁴ Yotuyanagi: Contribution of the Etiology and Pathogeny of Idiopathic Cystic Dilatation of the Common Bile Duct. Gann., 30, 601, October, 1936.
- ¹⁴⁵ Young: Glasgow Medical Jour., 107, 346, 1927.
- ¹⁴⁶ Zaczek: Congenital Cyst of the Common Bile Duct. Polski Przegl. Chir., 6, 639, 1927.
- ¹⁴⁷ Zimmer, H.: Zentralblatt für Chirurgie. 51, 424, 1924.
- ¹⁴⁸ Zininger and Cash: Congenital Cystic Dilatation of the Common Bile Duct. Arch. Surg., 24, 77-105, January, 1932.
- ¹⁴⁹ Zipf, K.: Über idiopathische Choledochuscysten. Arch. f. klin. Chir., 122, 615, 1922.

Note: For references for 42 of the cases taken from the Japanese literature, see the review by Yotuyanagi¹⁴⁴ (1936).

THE INDICATIONS FOR JEJUNAL ALIMENTATION IN THE SURGERY OF PEPTIC ULCER*

RALPH COLP, M.D., AND LEONARD J. DRUCKERMAN, M.D.

NEW YORK, N. Y.

FROM THE SURGICAL SERVICE, MOUNT SINAI HOSPITAL, NEW YORK, N. Y.

THIS REPORT comprises a series of 51 ward patients upon whom jejunostomy was performed for alimentation. This group consisted mainly of those in whom recurrent chronic peptic ulceration had left serious indelible physical imprints. The average age was 48, and the average duration of the disease was almost 12 years. Sixteen patients had experienced one or more attacks of severe gastro-intestinal hemorrhage. Many had been previously operated upon, 14 had been explored for an acute perforation of an ulcer, seven had had a gastro-enterostomy, and four a subtotal gastrectomy. Some of the patients were admitted to the hospital with a definite alkalosis, and others entered during an episode of severe hemorrhage. The accumulated experiences gained from a study of a group such as this, crystallized quite clearly, the indications for jejunostomy for alimentation in the surgery of peptic ulceration.

Jejunostomy was employed as a conservative preliminary procedure in uncontrollable alkalosis and in ulceration too extensive for immediate radical gastric surgery. It was established as a definitive palliative measure in those cases of severe peptic ulceration in which, because of certain physical conditions, any other type of surgery was deemed inadvisable. It was used quite frequently as a complement to gastric operations in a prophylactic effort to avoid the dire consequences of gastric atony, and finally, it was utilized as a supplementary procedure in those postoperative cases in which an intractable gastric ileus, with alkalosis developed.

PRELIMINARY JEJUNOSTOMY

This has been successfully employed by Balfour and Eusterman⁶ in those cases of massive gastric ulceration in which radical surgery was impossible at the time of operation. The benefits derived from this simple procedure were so marked that in many instances subtotal gastrectomy could be performed at a later period. Preliminary jejunostomy has been used in this clinic in some complicated cases of pyloric and duodenal stenosis with gastric dilatation. The symptom-complex of this condition was characterized mainly by repeated vomiting or the retention of large amounts of ingested food and gastric secretions. The inability to retain water, food and vitamins, and the loss of the acid secretion of the stomach caused fundamental alterations in the chemistry of the blood, notably an increase in the urea nitrogen, a diminution in the chlorides, and an increase in the carbon dioxide combining

* Read before the New York Surgical Society, December 9, 1942.

power. This pattern is called alkalosis. It has serious implications, for severe alkalosis is incompatible with life. Preliminary jejunostomy was performed for alimentation in six patients, because of a pronounced alkalosis which did not respond to the usual conservative therapy. The latter consisted of the parenteral administration of adequate amounts of saline and glucose which, as a rule, temporarily corrected the hypochloremia, provided that the kidney function was normal. The amount of salt in solution necessary to raise the lowered chloride content of the blood to normal limits may be measured by the formula of Coller, *et al.*⁴ The lowered serum proteins frequently found in the starvation incident to long-standing gastric obstruction were often effectively elevated by the administration of blood, blood plasma and amino-acids in sufficient quantities. In addition, the stomach was lavaged twice a day with hot saline solution in an effort to eliminate stagnation and diminish intragastric tension. This procedure often allayed the inflammatory reaction about an ulcer and relieved pylorospasm to such an extent that gastro-intestinal continuity was established and the stomach partially regained its tone. The efficacy of this treatment was gauged, empirically, by a reduction in the amount of gastric retention and, chemically, by a diminution in the degree of alkalosis. However, these conservative measures were found to be futile if persistent vomiting caused a constant loss of ingested food, fluid and gastric secretions. This type of high intestinal obstruction demanded surgical relief. Under these conditions, major gastric surgery was definitely contraindicated and, therefore, a preliminary jejunostomy for alimentation was performed under local anesthesia. Jejunal alimentation usually restored nutrition and hydration, and corrected alkalosis within a short period of time.

Beside the correction of the alkalosis and the subsequent improvement in the physical condition of the patient, a preliminary jejunostomy served other important functions. Jejunal alimentation, by eliminating gastric digestion, permitted the atonic stomach, now partially defunctionalized, to regain its tone and gradually contract. In addition, it allowed the local inflammatory reaction about an extensive penetrating ulcer to subside to such a degree that a subtotal gastrectomy could be performed eventually without undue risk.

The time intervening between the preliminary jejunostomy and subsequent gastric surgery varied. It was dependent upon the clinical improvement of the patient, the diminution in the amount of gastric retention, the amelioration of the alkalosis, and a recession in the extent of the local pathology, as demonstrated roentgenologically. The following cases illustrate these points:

Case 1.—Hosp. No. 448034: C. C., male, age 30, had suffered ulcer symptoms for ten years. He was operated upon for a perforation ten years ago. During the past six months he had vomited frequently and had lost weight. He had taken large doses of bicarbonate of soda the day of admission, October 31, 1939.

Physical examination disclosed generalized muscular rigidity, risus sardonicus, carpopedal spasm, and a positive Chvostek sign. The urine was alkaline, specific gravity

JEJUNAL ALIMENTATION

1.016, with a faint trace of albumin. Hemoglobin 63 per cent, carbon dioxide combining power 123.5 volumes per cent, chlorides, as sodium chloride, 340 mg. Blood urea 34 mg, calcium 8.5 mg., and phosphorus 5.8 mg. The gastric retention was 1,260 cc.

Course.—The patient was adequately treated with intravenous saline and glucose. He continued to vomit, and when treated with an indwelling tube, drained large amounts. Lavages did not materially decrease the gastric retention. The urinary specific gravity did not rise above 1.016. The blood carbon dioxide combining power and the chlorides approached normal limits but could not be kept there. It was felt that renal damage from a severe alkalosis, plus fluid and chloride loss from the stomach did not allow a more permanent correction of the alkalosis. It was, therefore, decided to perform a preliminary jejunostomy for alimentation. On November 10, 1939, exploration disclosed a huge, thin-walled stomach and a marked inflammatory reaction in the first portion of the duodenum. A typical Witzel jejunostomy was performed at a point 24 inches distal to the ligament of Treitz. Saline was given by drip into the

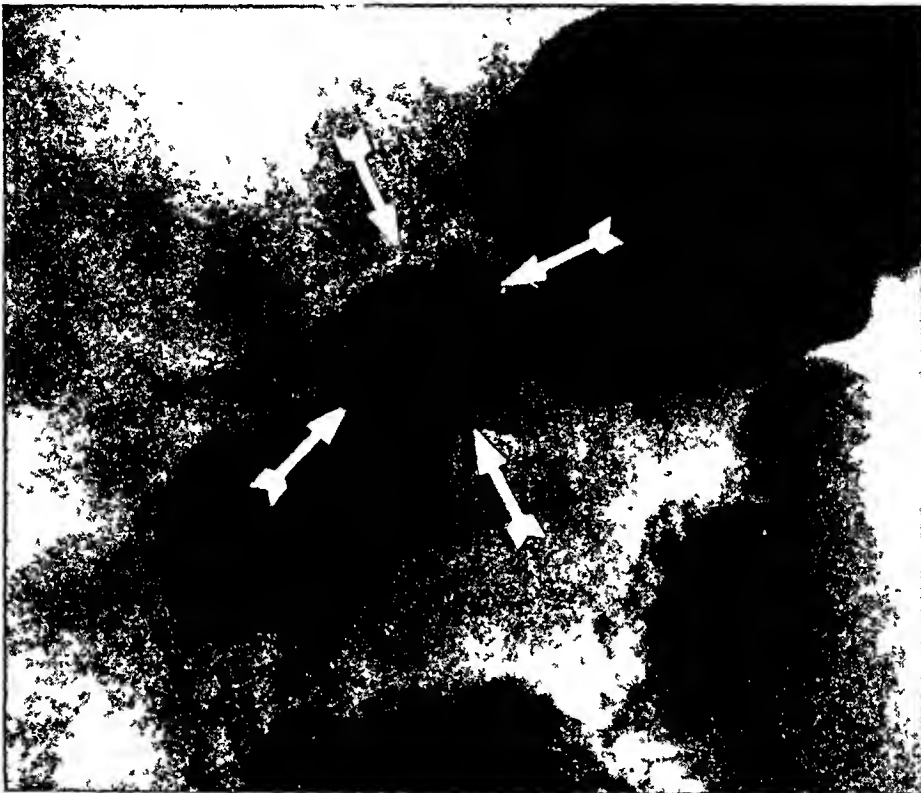


FIG. 1.—Case 2: Roentgenogram showing the large ulcer pocket.

jejunostomy tube and subsequently Scott-Ivy pabulum, vitamins, and Levin tube drainage in amounts up to 2,300 cc. daily. The patient had no cramps or diarrhea. He drained enormous amounts through the Levin tube at first. The intravenous drip which was being administered was stopped on the seventh postoperative day. The patient improved progressively. The blood chemistry figures returned to normal, and the urinary specific gravity rose to 1.020. He gained 13 pounds. By the eleventh postoperative day the gastric retention was only 30 cc. On the thirty-eighth postoperative day the patient was reoperated. A subtotal gastrectomy with an antecolic termino-lateral gastrojejunostomy of the Hofmeister type was performed. The jejunostomy was not disturbed. His postoperative course was remarkably uneventful. He was fed up to 1,800 cc. a day of Scott-Ivy pabulum. On the third and sixth day the patient had four diarrheal movements, which were controlled with small doses of deodorized tincture

of opium, administered through the jejunostomy. The tube was removed on the tenth day. The patient was discharged on the sixteenth postoperative day, very much improved.

He was seen in Follow-up Clinic, June 24, 1942, at which time he had no gastric complaints. He had gained ten pounds since discharge.

This case illustrates the efficacy of a jejunostomy performed in a patient suffering from a complete pyloric stenosis with huge gastric retention, resulting in severe alkalosis and kidney damage.

Case 2.—Hosp. No. 485954: B. D., male, age 37, entered the hospital, February 20, 1942, complaining of recurrent epigastric pain, relieved by food, for the past seven years. He had lost 45 pounds during this time. He was rather emaciated. The roentgenograms disclosed a markedly deformed duodenal bulb with a definite ulcer pocket, and gastric retention. Hemoglobin 78 per cent, blood chlorides 515 mg. as sodium chloride, carbon dioxide combining power 91 volumes per cent. The gastric retention was 1,200 cc.

Course.—The patient was treated with intravenous glucose and saline. Lavages were given, and, in the interim, a Sippy diet and amphogel. The pain and alkalosis, nevertheless, continued. The patient was explored under spinal anesthesia February 26, 1942. A greatly dilated stomach was found. There was a large mass in the first portion of the duodenum, apparently a penetrating duodenal ulcer. A typical jejunos-



FIG 2—Case 2. Roentgenogram after ten weeks of jejunal alimentation. The ulcer pocket is one third its former size.

tomy was performed. Postoperatively, the patient required parenteral fluids for three days only. Scott-Ivy pabulum and gastric drainage were given up to 2,000 cc. daily. Moderately severe cramps occurred on one occasion, but there was no diarrhea. The patient slowly improved, and as he retained a soft diet the jejunostomy feedings were diminished. The chemistry figures, however, never returned to normal. On the 74th postoperative day he was reoperated. The inflammation of the duodenum had decreased so that the swelling was one-third its original size (Figs. 1 and 2). A subtotal gas-

trectomy with an antecolic anastomosis was performed. The postoperative course was uneventful. Intravenous therapy was discontinued after three days. Scott-Ivy pabulum and saline were administered in amounts up to 1,900 cc. daily. The tube was removed on the seventh day. He was discharged 19 days after his second operation.

He was seen in Follow-up Clinic July 22, 1942. The patient had no gastric complaints, and he had gained 20 pounds.

This case illustrates the advantage of jejunal alimentation in the control of intractable pain and alkalosis. It demonstrates quite graphically the partial subsidence of the local inflammatory reaction, and the diminution in the size of the stomach.

Case 3.—Hosp. No. 481601: F. G., male, age 44, had suffered pain, relieved by food, for five years. He had had a severe gastro-intestinal hemorrhage three years ago, and since then had milder attacks of bleeding at three- or four-month intervals. During the last five months the pain had become more severe, and was unrelieved by alkalis. In the past week the pain had increased, and he had noticed black stools. Vomiting was present for two days prior to admission November 10, 1941.

Physical examination disclosed a pale, emaciated male. There was moderate epigastric tenderness and spasm. The stool was tarry. Pulse 120; blood pressure 115/85. Hemoglobin 50 per cent. Blood urea 22 mg.; chlorides 515 mg.; carbon dioxide combining power 89 volumes per cent. He had a gastric retention of 1,900 cc.

Course.—Despite medical treatment and parenteral fluids, he continued to vomit and suffer pain. The bleeding stopped. The blood chemistries varied, and four weeks after admission, in spite of parenteral fluids, the blood carbon dioxide combining power was 105 volumes per cent, chlorides 455 mg., and urea 36 mg. Therefore, a typical preliminary jejunostomy was performed under spinal anesthesia December 9, 1942. Postoperatively, amounts of Scott-Ivy pabulum and gastric drainage were given up to 2,600 cc. daily. The blood chemistry, however, never reached normal. During a period of several weeks he was fed a Muelengracht diet and given atropine, but he continued to have occasional negative oral balances, and one episode of melena. With repeated transfusions the hemoglobin was brought up to 74 per cent. Exploration was performed under spinal anesthesia February 5, 1942. The stomach was twice normal size. Just beyond the pylorus was a marked constriction due to a posterior wall ulcer. A typical subtotal gastrectomy with an antecolic anastomosis was performed. The negative oral balances stopped after the fourth postoperative day. About 3,000 cc. of gastric aspiration and Scott-Ivy pabulum were given daily. Tube was removed on the fourteenth day. The patient was discharged on the sixteenth day.

He was seen in Follow-up Clinic four months later. He had no gastric complaints, and had gained 48 pounds.

This case illustrates the efficacy of enteral alimentation as opposed to parenteral hydration and alimentation in controlling a marked tendency toward alkalosis. It also discloses the fact that if a patient is properly prepared, the postoperative course for a long time after a bleeding episode will be uneventful.

Jejunostomy in these cases was always followed by a subtotal gastrectomy.

PALLIATIVE JEJUNOSTOMY

Jejunostomy as a definitive procedure in the surgery of gastroduodenal ulcer has outlived its usefulness. It has little to recommend it at present. It was only employed in those exceptional cases in which the general

physical condition of the patient and the characteristics of the local pathology permanently contraindicated any subsequent gastric surgery. The effects of palliative jejunostomy in these cases were similar to those obtained by the use of preliminary jejunostomy, but, inasmuch as further corrective surgery is prohibited, the clinical benefits will last only as long as the alimentation is continued. In one case (Hosp. No. 464135), jejunostomy was performed for an acute jejunal ulcer which developed after an extremely high subtotal gastrectomy and anterior vagotomy. Insufficient stomach remained for any further resection. The jejunal alimentation was continued for 96 days, and the patient improved. However, the ultimate prognosis is extremely doubtful. The second patient (Hosp. No. 482627) was a woman well advanced in years and afflicted with hypertension and cardiovascular disease. Following a gastro-enterostomy she developed a severe, bleeding, gastrojejunal ulcer which almost completely occluded the stoma and resulted in marked gastric retention with alkalosis. A palliative jejunostomy was performed 19 months ago, and the tube is still in place. Generally, she has improved. However, on occasions the ingestion of food causes episodes of gastric distress and bleeding. A return to the jejunal feedings relieves the symptoms. It is likely that if the tube is ever permanently removed there will be a return of the jejunal ulceration.

COMPLEMENTARY JEJUNOSTOMY

The largest number of jejunostomies for alimentation in this series has been the complementary type, those which were performed coincidentally with the gastric operation. This was done with the hope that it might neutralize many of the postoperative difficulties in gastric emptying. Some of the mechanisms involved in the pathologic physiology of atony of the stomach are not definitely known. Cases of acute gastric dilatation may be secondary to mechanical factors. Obstruction may be caused by an occluding edema of the gastro-enteric stoma which is often inflammatory at first, and subsequently is abetted by the biochemical disturbances incident to hypoproteinemia.^{8, 11} Occasionally an acute obstruction may develop in a retrocolic gastro-enterostomy because of a prolapse of the stoma or the efferent loop into the lesser omental sac. In a few cases, the postoperative development of a plastic exudate and adhesions may be sufficient to occlude either the afferent or efferent jejunum. However, there are cases of acute gastric dilatation or atony in which neither operative exploration nor postmortem examination reveals any anatomic cause for the clinical symptomatology of obstruction. This type of gastric ileus has been attributed to many factors. Any operative procedure upon the stomach, regardless of the technical skill of the surgeon, is accompanied by a certain amount of unavoidable trauma often causing muscular paresis and atony. In addition, a subtotal gastrectomy which entails the excision of a greater part of the lesser curvature and partial destruction of the gastrohepatic omentum causes considerable

damage to the vagus nerve. This adversely affects the motor activity of the stomach. Moreover, in those cases in which the stomach has been previously dilated, there is no reason to assume that any anastomotic procedure or radical gastric resection will immediately remedy the atony. It is a common experience following a gastro-enterostomy or a gastric resection that 24 to 48 hours may elapse before the stomach partially regains its peristaltic activity. The inevitable sequela is the stagnation of gastric contents causing repeated vomiting, or persistent gastric drainage through an indwelling Levin tube.

Fortunately, however, in the majority of patients these difficulties in gastric emptying are transient and inconsequential. If they persist, they portend serious consequences. The daily loss by vomiting or gastric drainage of several thousand cubic centimeters of ingested fluids, gastric and duodenal secretions, rapidly causes dehydration, inanition, avitaminosis, hypoproteinemia and alkalosis. These chronically ill individuals need adequate and proper nourishment from the very beginning of their postoperative period. This is not completely supplied in some patients by the parenteral administration of blood, plasma, vitamins, amino-acids and electrolytes. It is the systemic effects produced by gastric atony in its varying severity and duration which adds to the morbidity and mortality of gastric surgery.

Inasmuch, as gastric atony is always a potential postoperative complication, prophylactic operations have been devised to eliminate its consequences. These procedures have been reviewed in detail by Perman.¹⁰ Any method to be effective in the treatment of gastric atony must fulfill certain requirements. It must keep the dilated stomach decompressed, it must provide adequate fluid and nourishment during this period of gastric inactivity, and it must prevent alkalosis. It would seem that the two-way gastro-enterostomy tube developed by Abbott and Rawson¹ would satisfy these desiderata. However, the use of this tube in our experience has not been satisfactory. Its introduction from the stomach into the efferent jejunal loop during a subtotal gastrectomy is not an easy procedure, especially if asepsis is to be maintained. Moreover, during the postoperative period it may be inadvertently dislodged either by an uncooperative patient or through carelessness. Furthermore, these tubes cannot be kept in place indefinitely because of the danger of damage to the arytenoid cartilages. We have seen two cases in which an edema of the larynx developed from an arytenoiditis. If the two-way tube were entirely satisfactory in the decompression of the stomach and in the simultaneous maintenance of nourishment, jejunostomy for alimentation would not have been recently revived in gastric surgery. This is evidenced by the papers of Wesson,¹⁴ Allen and Welch,² and Clute and Bell.³

In 1929, Kirschner⁹ advocated the complementary use of jejunostomy in gastroduodenal surgery, and he utilized this procedure in 60 cases of subtotal gastrectomy. He reported that it was extremely useful. It supplied immediate nourishment to those who had suffered so long from an ulcer that

their capital resources had already been drawn upon for their sustenance. Moreover, the deleterious and dire consequences of a gastric ileus was often neutralized by the complementary jejunostomy.

The importance and the practical applications of Kirschner's contribution evidently have not been fully appreciated. Since 1938, we have used complementary jejunostomy in an increasing number of patients with gratifying results. Indications have been gradually established so that it is now employed routinely in certain types of cases. It was used in those gastric and duodenal ulcers which were complicated by stenosis and marked gastric dilatation, for, as has been stated previously, a stomach which has been atonic prior to operation is likely to be atonic following operation. Complementary jejunostomy was especially helpful in those instances in which the technical procedures were unusually traumatic or complicated, as in extensive resections for gastrojejunal ulcers or those at the cardia. These patients were found to be especially prone to gastric ileus. Another indication for the use of concomitant jejunostomy was found in those cases in which a dehiscence of a friable duodenal stump was a possibility. These were drained routinely, and if a fistula developed the duodenal contents were aspirated by suction and fed together with the pabulum *via* the jejunostomy. In this way the nutrition and normal chemical balances were usually maintained. Complementary jejunostomy has been performed in 38 cases. It was used in 11 cases of gastro-enterostomy and in 21 of subtotal gastrectomy. In four instances it was established simultaneously with a resection of the stomach following either a previous gastrectomy or a gastro-enterostomy. In one case it was performed as a coincident procedure to the restoration in continuity for a gastrojejunocolic fistula, and in another patient it was used as an aid to an entero-anastomosis for a stenosing ulcer of the afferent jejunum.⁵ It is undoubtedly true that complementary jejunostomy was unnecessary in some cases, as judged by the subsequent postoperative course. However, even in these patients it did no harm and certainly simplified the postoperative alimentation and diminished considerably the period of time in which intravenous therapy was required.

The following cases, which are abstracted, demonstrate the efficacy of complementary jejunostomy:

Case 4.—Hosp. No. 457630: I. S., male, age 58, was admitted, June 1, 1940, because of epigastric pain, eructations and vomiting of 25 years duration. Examination disclosed an edentulous male. There was tenderness in the upper abdomen, and a definite succussion splash could be elicited. The hemoglobin was 84 per cent, blood chlorides 410 mg., and carbon dioxide combining power 74 volumes per cent. There was 2,200 cc. of retained food and fluid in the stomach. Roentgenologic examination showed a marked deformity of the duodenal bulb and an ulcer pocket on the lesser curvature side. There was a delay in gastric emptying. Thirty-five per cent of the barium was retained after six hours.

The patient was prepared for operation with intravenous saline and glucose, lavages, and vitamins, for 16 days. On June 17, 1940, exploration, under cyclopropane anesthesia, disclosed a large duodenal ulcer perforating into the head of the pancreas. A typical subtotal resection and jejunostomy for alimentation was performed. Post-

operatively, the patient developed a typical gastric atony, which persisted for 16 days. During this time alimentation was maintained by feeding Scott-Ivy pabulum and Levin tube drainage through the jejunostomy in amounts up to 2,500 cc. daily, augmented by intravenous saline and glucose and transfusions. On the eleventh postoperative day roentgenograms disclosed complete retention of barium in the stomach after 25 hours (Fig. 3). The atony subsided after the sixteenth day and the patient improved



FIG. 3.—Case 4: Roentgenogram taken on eleventh postoperative day, 25 hours after the administration of barium. Note that none has left the stomach. The jejunostomy tube is seen *in situ*.

rapidly. On the twenty-fifth day roentgenograms disclosed a normally emptying stomach (Fig. 4). The tube was removed on the twenty-second day and he was discharged on the twenty-sixth postoperative day.

This case illustrated the fact that preoperative gastric atony is not relieved by resection, but rather that the ileus continues. The importance and convenience of a jejunostomy for alimentation is readily appreciable.

Case 5.—Hosp. No. 453628: G. C., male, age 72, had originally entered the hospital because of recurrent indigestion, epigastric pain, vomiting and bleeding, in August,

1939. Roentgenograms disclosed a deformed bulb with marked delay in emptying time. He was transfused several times. His blood urea rose to 118 mg, and the specific gravity of the urine remained low, about 1.006. It was felt that these changes represented kidney damage due to alkalosis incident to the vomiting and prolonged ingestion of bicarbonate of soda. He was discharged much improved, only to be readmitted several months later with an acute perforation of his ulcer. This was sutured, and the patient recovered. On May 12, 1940, he was readmitted because of weakness, anorexia, and burning pain in the epigastrium. Examination disclosed an elderly, emaciated male



FIG. 4.—Case 4: Roentgenogram taken on twenty fifth postoperative day disclosing a normally emptying stomach.

deaf-mute. There was general epigastric tenderness and evidences of marked arteriosclerosis. Hemoglobin was 40 per cent Blood carbon dioxide combining power 63.1 volumes per cent, and chlorides 595 mg. There were 2,000 cc. of gastric retention. The patient was transfused several times, and was lavaged frequently. He continued to have many attacks of epigastric pain, some of which were relieved by removing large quantities of gastric retention.

Course.—On April 15, 1940, under local anesthesia, the patient was explored. The stomach was found to be twice normal size, and there were multiple adhesions in the region of the duodenum. In the first portion of the duodenum there was a scar

and contraction due to the duodenal ulceration. A typical posterior gastro-enterostomy was performed, and a tube-jejunostomy established 12 inches below the anastomosis. Postoperatively, the patient had large negative oral balances for 12 days. He was fed Scott-Ivy pabulum in increasing doses up to 2,880 cc. daily, without diarrhea or cramps. An intravenous was necessary for four days only. His blood chemistry values remained normal. The urinary output was good. The tube was removed on the nineteenth postoperative day, and the wound healed promptly.

He was seen in the Follow-up Clinic, July 22, 1942, at which time he had gained 25 pounds, and had suffered no gastric complaints.

This case is typical of the excellent results obtained from the establishment of a jejunostomy for alimentation in a seriously ill, elderly male, who had suffered long-continued gastric dilatation due to obstruction, and in whom it was to be expected that a postoperative gastric ileus would develop. It is typical of the advantages of the complementary jejunostomy.

SHORT ABSTRACTS

Case 6.—Hosp. No. 454659: B. L., male, age 40, had suffered peptic ulcer disease for six years, and had been repeatedly admitted to the hospital for pain, vomiting, perforation and alkalosis. At operation, his stomach was found three times normal size. A subtotal resection and jejunostomy for alimentation were performed. Postoperatively, his course was uneventful except that he had persistent negative oral balances, as high as 2,150 cc. daily. He was fed large amounts, up to 3,450 cc., of Scott-Ivy pabulum daily. The negative oral balance continued for nine days. The tube was removed on the thirteenth day, and the patient discharged on the fourteenth day.

Case 7.—Hosp. No. 468543: H. H., male, age 41, had suffered ulcer symptoms, including one episode of perforation, for 13 years. He entered the hospital after several months of vomiting. Gastric retention was 2,100 cc. At operation, an enormous dilatation and hypertrophy of the stomach, and a large inflamed duodenal ulcer were seen. A typical subtotal resection and jejunostomy were performed. The patient continued, postoperatively, to have negative oral balances for 14 days. He was fed up to 1,700 cc. of pabulum daily, and this, as well as intravenous saline, glucose, and amino-acids, did much to help him through the prolonged period of gastric atony.

Case 8.—Hosp. No. 480134: S. B., male, age 41, entered the hospital for surgical treatment of a penetrating jejunal ulcer. A secondary subtotal resection and a jejunostomy were performed. The patient had a negative oral balance for nine days and was fed pabulum, Levin tube drainage, vitamins and sulpha drugs through the jejunostomy tube. Despite a rather severe postoperative pneumonia, he recovered.

Case 9.—Hosp. No. 465396: A. K., male, age 40, upon whom a high subtotal resection, with a Murphy button anastomosis, was performed because of a highly situated lesser curvature ulcer. Postoperatively he had a negative oral balance for 11 days, and was tided through this difficult period by large amounts of jejunostomy feedings and replacement of Levin tube drainage.

Even in this small series, it becomes quite apparent that if a concomitant jejunostomy had not been performed, a supplementary jejunostomy would probably have been necessary in some cases because of a persistent gastric ileus. These cases, from reports in the literature, are always attended by an appreciable mortality.

SUPPLEMENTARY JEJUNOSTOMY

Naturally, there are cases in which the possible occurrence of a gastric atony following operative procedures upon the stomach cannot be predicted.

Severe gastric atony in some patients may occur from the very beginning; in others it may not become evident until a week or ten days after operation. The clinical picture, however, is similar in both groups of cases. It is recognized by the symptoms and the physical findings of a high intestinal obstruction, in which progressive deterioration occurs in spite of adequate parenteral treatment. There is always a tendency to procrastinate too long with conservative therapy, reserving operative intervention until it is too late. This is undoubtedly the reason that the results of secondary procedures in these cases are attended by such a prohibitive mortality. When gastric ileus was suspected because alkalosis and increasing or stationary large negative oral balances were present, roentgenologic examination of the stomach with barium proved to be invaluable and indispensable. It revealed a dilated stomach in which the barium was completely retained, or it disclosed other reasons for the obstruction, as, for example, an occlusion of the efferent jejunum. We agree with the conclusions of Allen and Welch,² that in the older-age group of patients exploration should be undertaken after seven days if the amounts obtained by gastric aspiration show a stationary or progressive increase and the chemical evidences of alkalosis are present. In younger patients conservative measures may be tried for a longer period of time.

Many operative measures have been advocated to correct or relieve the effects of gastric atony. Surgeons have advised another gastro-enterostomy when a malfunction of the previous one was suspected. This usually is futile. Entero-enterostomy has been suggested if there is a marked dilatation of the afferent loop in contrast to a contraction of the efferent jejunum. This rarely relieves gastric atony and, moreover, it subsequently deprives the stomach of the full benefits of duodenal alkalization. Hoag and Saunders⁷ reported several cases in which a gastric ileus was relieved by jejunoplasty performed in the region of a malfunctioning gastro-enteric stoma. Many Continental surgeons have been enthusiastic in their praise of a tube-gastrostomy. However, similar benefits are obtained by the routine postoperative use of continuous suction drainage of the stomach.

Supplementary jejunostomy for alimentation in cases of gastric atony was suggested at a very early period in the development of gastric surgery.¹³ In our experience, it has proven to be most satisfactory. It is a simple technical procedure which can be performed through the original operative incision expeditiously and without shock. To repeat, it is a method which, when combined with the concomitant use of gastric drainage, decompresses the stomach, maintains nutrition, and corrects alkalosis.

The following cases are of interest:

Case 10.—Hosp. No. 467016: J. M., male, age 25, was admitted, December 27, 1941, complaining of epigastric pain, relieved by food or soda, of five years duration. Two years ago he had an episode of bleeding, and one year ago a perforation of a duodenal ulcer was sutured. Three days prior to admission he noticed a tarry stool, and subsequently fainted. He had had poliomyelitis in childhood, and had been left with a

partial paralysis of the right upper and both lower extremities, despite numerous corrective operations.

Physical examination disclosed a pale young male. There was moderate epigastric tenderness. The hemoglobin was 52 per cent, and the blood chemistries were normal.

Course.—The patient was transfused repeatedly. The stools became guaiac-negative, and the hemoglobin rose to 75 per cent. On January 15, 1942, under spinal anesthesia, a subtotal gastrectomy with antecolic anastomosis was performed for an active duodenal ulcer with stenosis. Postoperatively, from the beginning the Levin tube drained large amounts. Despite adequate parenteral therapy, alkalosis developed. The blood carbon dioxide volume power rose to 83.2 volumes per cent, and the blood chlorides to 540 mg. prior to operation. On February 2, 1942, under spinal anesthesia, the median incision was reopened and the operative site examined. No organic cause for obstruction was found. A purse-string jejunostomy was performed. Postoperatively, the patient developed an active phlebitis of the dorsum of the right hand, and suffered chills and high fever. Blood culture was positive for a gram-negative bacillus. The sepsis subsided with chemotherapy. He continued to vomit. On the seventh postoperative day blood chemistries showed carbon dioxide combining power 58.4 volumes per cent, chlorides 620 mg., urea 9 mg. Through the jejunostomy he was given up to 3,200 cc. of Scott-Ivy pabulum, gastric drainage, saline and sulfathiazole for 18 days. One mild episode of diarrhea was controlled by the administration of tincture of opium. The patient had a negative oral balance for 13 days after jejunostomy (a total of 31 days after the original gastrectomy). After the eighteenth day, alimentation was entirely oral. The jejunostomy tube was removed on the twenty-fourth day, and he was discharged.

He was seen in the Follow-up Clinic, October 28, 1942, at which time he was in excellent health.

This patient also illustrates the value of the supplementary jejunostomy for a gastric ileus, which persisted 31 days after gastrectomy. Because of a marked phlebitis and sepsis, parenteral therapy was impossible, and jejunostomy alone controlled the alkalosis and maintained nutrition.

Case 11.—Hosp. No. 484235: D. W., male, age 50. Thirteen years ago, following an episode of melena, a perforation of a duodenal ulcer occurred. This was sutured, and since then he has suffered epigastric pain relieved by food and soda. Roentgenologic examination on admission disclosed a large penetrating duodenal ulcer. The blood chemistries were normal.

Course.—Exploration, under spinal anesthesia, January 19, 1942, disclosed a dilated stomach, with a marked deformity of the duodenum and a small diverticulum. A typical subtotal gastrectomy with antecolic anastomosis was performed. Postoperatively, from the beginning, the patient drained large amounts through the Levin tube, and vomited when it was removed. Hydration was maintained by the intravenous route. The carbon dioxide combining power rose to 84 volumes per cent by the fifth postoperative day. Inasmuch, as the negative oral balance varied between 2,500 and 3,000 cc. per day, exploration was deferred until the seventh postoperative day.

On January 26, 1942, under spinal anesthesia, and through a left rectus incision, the operative site was examined and found to be normal. Eighteen inches distal from the anastomosis a typical Witzel jejunostomy was performed. The patient was subsequently fed up to 88 ounces daily of Scott-Ivy pabulum, vomitus, Levin tube drainage and vitamins. The carbon dioxide combining power dropped to 59.2 volumes per cent on the fourth postoperative day. He developed a right upper lobe pneumonia, which responded to chemotherapy. A dehiscence of the left rectus incision was treated by packing.

This patient continued to have a negative oral balance for 13 days following the supplementary procedure. During this period alimentation was maintained by jeju-

nostomy which, together with intravenous amino-acid, kept the blood proteins within normal limits. Twenty-five days after the second operation the jejunostomy tube was removed. The wound healed rapidly, and he was discharged February 22, 1942.

He was seen in Follow-up Clinic, April 22, 1942, at which time he had no gastric complaints, and felt quite well.



FIG. 5.—Roentgenogram disclosing complete obstruction at site of a Witzel jejunostomy.

This case illustrates the proper employment of the supplementary jejunostomy. When the gastric ileus showed no signs of abating, and alkalosis progressed despite intravenous therapy, the patient, who was age 50, was promptly explored. No organic cause for the obstruction was found. A jejunostomy was performed with excellent results.

JEJUNAL ALIMENTATION

THE TECHNIC OF JEJUNOSTOMY AND JEJUNAL ALIMENTATION

The history and clinical application of jejunostomy for alimentation has been thoroughly and adequately reviewed by Wolfer.¹⁵ The technic employed for jejunostomy in this clinic was quite simple, and added but a few moments to the operative time, when performed coincidentally with a gastric procedure. If the jejunostomy was preliminary, a median epigastric incision was made from the ensiform to the umbilicus, under spinal or local anesthesia. This exposure afforded ample opportunity to explore the upper abdomen and gave easy access to the identification of the duodenojejunal angle. The intestine was traced distally for about 18 to 24 inches from the ligament of Treitz. If a loop of bowel is picked at random in the left upper quadrant on the assumption that it is high jejunum, the operator may be dismayed when he subsequently finds, at postmortem examination, that he has performed a low ileostomy.

The Witzel type of jejunostomy was performed in the first 39 cases. There were two complications, one, an instance of acute intestinal obstruction which developed at the site of the jejunostomy and necessitated operative intervention (Fig. 5.) (Hosp. No. 480550), and in the other patient the signs of local peritonitis developed in the region of the enterostomy. This subsided with the removal of the tube.

Recently, impressed by the experiences of others,^{2,3} we have performed the operation in 12 cases according to the Stamm principle. Through a small opening in the jejunum, a No. 12 to 14 F. whistle-tip catheter was fed aborally for about six inches. The tube was then fixed to the bowel with catgut and was buried by means of two purse-string linen sutures. The patency of the jejunostomy was tested immediately by the introduction of saline. The catheter was simply brought through a stab wound in the left subcostal region and attached to the skin with silk.

Four hours after operation 60 cc. of warm saline was introduced, and this was repeated every two hours. After 12 hours 60 cc. of the Scott-Ivy¹² pabulum, alternating with saline, were given regularly. The amount was gradually increased to 120 cc., or more, hourly. The Scott-Ivy pabulum, which is usually well tolerated by the jejunum, is a nonirritating mixture of high caloric content and necessary food elements. The feedings, which are warmed, are given slowly, preferably by gravity drip, or by syringe. If given too rapidly or in too large quantities, jejunal regurgitation may occur. This is easily recognized because, if suspected, insoluble carmine may be mixed with the pabulum and recovered in the gastric drainage. In about ten per cent. of the cases, these feedings caused diarrhea and cramps, which were usually controlled by appropriate doses of tincture of opium and bismuth subcarbonate. Amino-acids and medications have also been given by jejunostomy. The tube occasionally became plugged, but the obstruction was relieved by irrigation with a ureteral catheter. When the loss of gastric contents through the indwelling tube was appreciable,

the drainage was collected and part of it was introduced through the jejunostomy, alternating with the pabulum feedings. Jejunal alimentation was continued until the stomach emptied normally. The tube was removed, as a rule, 48 hours after the jejunal feedings had been discontinued. The earliest removal in the complementary cases was nine days, the latest 35 days, and the average 15 days. Although there was some drainage of bile for 24 hours, or more, after its removal, the discharge soon ceased spontaneously in both the Witzel and Stamm types of jejunostomy.

Jejunostomy *per se* did not account for a single mortality in this series.

SUMMARY

1. Jejunostomy for alimentation was performed in a series of 51 patients suffering from recurrent chronic peptic ulcer.

2. It was used as a preliminary, palliative, complementary, and supplementary measure in the surgery of gastroduodenal ulceration. The indications and clinical applications of these are fully described.

3. The technic of jejunostomy and jejunal alimentation is discussed.

4. Evaluation of results obtained.

REFERENCES

- 1 Abbott, W. O., and Rawson, A. J.: A Tube for Use in Postoperative Care of Gastro-enterostomy Patients. *J. A. M. A.*, 112, 2414, 1939.
- 2 Allen, A. W., and Welch, C. E.: Jejunostomy for the Relief of Malfunctioning Gastro-enterostomy Stoma. *Surgery*, 9, 163, 1941.
- 3 Clute, H. M., and Bell, L. M.: Jejunostomy for Postoperative Feeding. *ANNALS OF SURGERY*, 114, No. 3, 402, 1941.
- 4 Coller, F. A., Bartlett, R. M., Bingham, L. C., Maddock, W. G., and Pedersen, S.: The Replacement of Sodium Chloride in Surgical Patients. *ANNALS OF SURGERY*, 108, 769, 1938.
- 5 Colp, R.: Surgical Problems in the Treatment of Gastrojejunal Ulceration. *ANNALS OF SURGERY*, 114, 543, October, 1941.
- 6 Eusterman, G. B., and Balfour, D. C.: The Stomach and Duodenum. W. B. Saunders, Philadelphia, 1936.
- 7 Hoag, C. L., and Saunders, J. B.: Jejunoplasty for Obstruction Following Gastro-enterostomy or Subtotal Gastric Resection. *Surg. Gynec. and Obst.*, 68, 703, 1939.
- 8 Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema. *Arch. Surg.*, 27, 159, 1933.
- 9 Kirschner, M.: Die Prophylactische Jejunostomie bei Magenoperationen. *Arch. f. klin. Chir.*, 157, 561, 1929.
- 10 Perman, E.: Surgical Treatment of Gastric and Duodenal Ulcer. *Acta. Chir. Scand.*, 77, suppl. 38.
- 11 Ravdin, I. S.: Factors Involved in the Retardation of Gastric Emptying after Gastric Operations. *Penn. M. J.*, 41, 695, 1938.
- 12 Scott, H. G., and Ivy, A. C.: Jejunal Alimentation. *ANNALS OF SURGERY*, 93, 1197, 1931.
- 13 Stieda, A.: Über die Vorbereitung und Nachbehandlung bei Magenoperationen. *Arch. f. klin. Chir.*, 63, 715, 1901.
- 14 Wesson, H. R.: Postoperative Gastric Retention Treated by Jejunostomy for Feeding. *Proc. Mayo Clin.*, 12, 727, 1937.
- 15 Wolfer, J. A.: Jejunostomy with Jejunal Alimentation. *ANNALS OF SURGERY*, 101, 708, 1935.

DIVERTICULA AND VARIATIONS OF THE DUODENUM

WOLFGANG ACKERMANN, M. D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY,
NEW YORK, N. Y.

IN THE REGIONAL ANATOMY COURSE given to third year medical students at the College of Physicians and Surgeons no difficulty was encountered in demonstrating anomalies of the abdominal viscera except as to diverticula of the duodenum. It seemed reasonable to assume that such abnormalities might elude observation, especially when they are small or embedded in the pancreatic tissues. To overcome this obstacle the idea was advanced that making casts of the duodenum would be a reliable method of demonstrating them.

The ideal material for this purpose appeared to be "Korogel," a molding jelly. However, because of certain technical difficulties connected with the handling of it, plaster of paris was used instead, and it proved entirely satisfactory.

A few experiments were first made on cadavers in the Departments of Anatomy and Pathology. Then, with the beginning of the school year 1938-1939 and through 1940-1941, every cadaver that came to the laboratory for use by Dr. Allen O. Whipple in teaching surgical anatomy, was examined for the presence of duodenal diverticula. During that period 50 bodies were studied. They were not selected, but taken at random.

PROCEDURE: When the abdomen is opened and the study of the viscera is about to begin, the omentum with the transverse colon and stomach are lifted up and turned back. The pylorus is mobilized, a piece of cord is passed underneath and tied snugly around it. The duodenum is left *in situ*. The duodenojejunal junction is located and a piece of cord is passed beneath through the mesentery. The jejunum is incised transversely on its anti-mesenteric border, about one inch below its junction, just enough to permit the insertion of an adapter to an all-metal 250 cc. syringe. The jejunum is now tied once over the adapter with the cord placed beneath it. The syringe is filled with plaster, which is injected slowly, exerting only sufficient pressure to ensure its entering any recess or diverticulum that may be present.

When the duodenum is filled to its capacity, the plaster commences to flow back. Then, as the syringe with its adapter is being quickly removed, an assistant ties a second knot to prevent the reflux.

After the plaster hardens sufficiently, the common duct is probed for its patency and then injected with about two to three centimeters of methylene blue, to establish the relation of the ampulla of Vater to the duodenum. The following day the duodenal wall is incised along its entire convex

border and the model is removed with great care, while both the interior of the duodenum and the cast are being studied.

It is not within the scope of this paper to discuss, in detail, classification, etiology, age and sex incidence, size, location, distribution, *etc.*, of duodenal diverticula. With regard to such particulars the reader is referred to the literature. However, it must be pointed out that all diverticula herein described belong to the *primary* group, meaning those which have no obvious cause for their appearance, in contrast to those which are produced for instance by ulcers or adhesions and are called *secondary*, *true*, or *acquired*.

The *primary* are also called *false* or *congenital*. Although not proven, they are congenital in their nature, as they represent abortive attempts at the formation of a supernumerary pancreas. The pancreatic anlagen cause local defects in the musculature and the possibility of pouching results from age, intestinal atony or an increase of intraduodenal pressure. This view is the opinion of Letulle, Tandler, Falconer, Lewis and Thyng.

Illustrations of 11 specimens (Figs. 1-11) among a total of 50 show single or multiple diverticula. This is 22 per cent, the highest figure so far recorded.

Although Grant is of the opinion that percentages convey little if any information, unless the statement bears with it reference to age, this is believed to be true only from the theoretic point of view. Clinically speaking, one must consider duodenal diverticula in differential diagnosis regardless of the age, since they occur at all ages.

The total number of the diverticula found is 14, if one bilocular (*a* and *b* of Fig. 2), meaning a combination of two diverticula with a common orifice, *c*, is accepted as a single diverticulum.

Of the 11 specimens with diverticula, eight (Figs. 1, 3, 5, 6, 7, 8, 9 and 11) had one, and three (Figs. 2, 4 and 10) had two diverticula.

The distribution is as follows: Five diverticula in the second part of the duodenum (*a-c*, of Fig. 2, Fig. 3, *a* and *b* of Fig. 4, and Fig. 5); one between the second and third parts (Fig. 6); five in the third part (*d* of Fig. 2, Figs. 7, 8, 9 and *a* of Fig. 10); and three in the fourth (Fig. 1, *b* of Fig. 10, and Fig. 11). Thus, the opinion of practically all writers that the greatest number of diverticula occur in the second part cannot be corroborated by the findings recorded in this paper.

No diverticula were found in the first part; and all sprang from the concave, pancreatic border, which is morphologically the mesenteric border of the duodenum. All but four (*a-c* of Fig. 2, *d* of Fig. 2, Fig. 3 and *a* of Fig. 4) were buried in the substance of the pancreas, and had they not been filled with plaster a number of them would certainly have escaped detection.

As to their shape, it is obvious that the greater number are globular; some are funnel-shaped and some cylindrical.

The dimensions of the diverticula given in the Figures are probably

DUODENUM DIVERTICULA

FIG. 1.



FIG. 2.

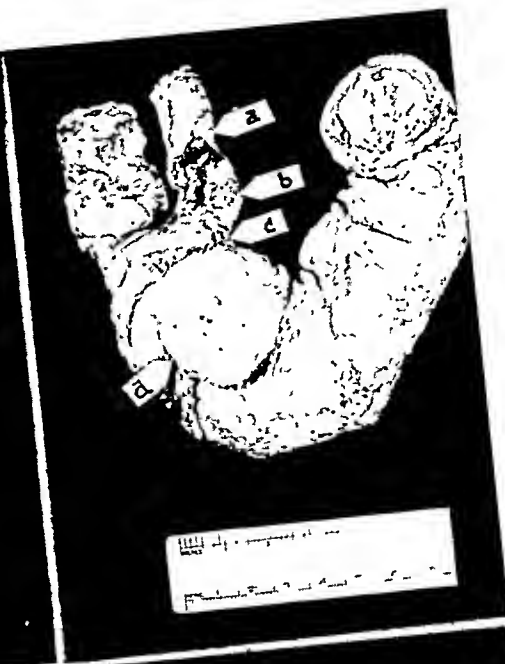


FIG. 3.



FIG. 4.

FIG. 1.—Arrow points to a small diverticulum in the fourth part of the duodenum, the smallest in the series.

FIG. 2.—The specimen shows a bilocular diverticulum *a* and *b*, arising from a common orifice *c* in the second part. Diverticulum *b* projects anteriorly and is, therefore, not demonstrated distinctly in the photograph. A second diverticulum is seen at *d*, in the third part of the duodenum. It is large, globular, and like the bilocular it arises on the pancreatic border; anteriorly, it appears to have a flat, smooth surface, a condition caused by the presence of air at the time of casting it.

FIG. 3.—A single diverticulum of the second part has a fairly large orifice. The arrow points to the location of the papilla of Vater.

FIG. 4.—Two diverticula are seen, both in the second part; diverticulum *a* extends medially and anteriorly, and diverticulum *b* posteriorly.

FIG. 5.



FIG. 6.

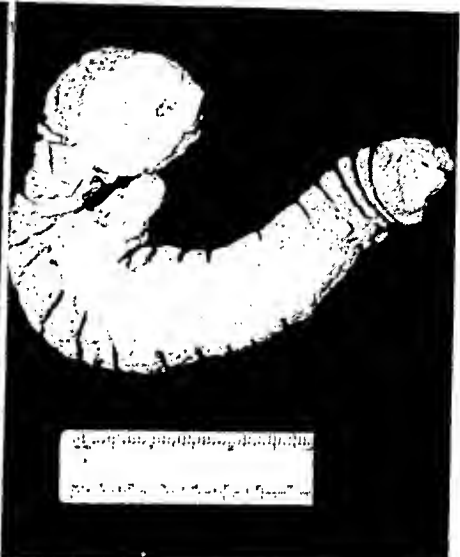


FIG. 7.



FIG. 8.

FIG. 5.—The first part of the duodenum is large, the second and fourth parts are short. A single diverticulum may be seen at the lower end of the second part.

FIG. 6.—A fairly large diverticulum with a broad opening appears at the junction of the second and third parts of the duodenum.

FIG. 7.—The diverticulum in the third part of the duodenum is large and has a narrow orifice. The arrow points to the location of the papilla of Vater.

FIG. 8.—This is the smallest duodenal cast in the series. The diverticulum in the third part has a narrow orifice. The arrow indicates the location of the papilla of Vater.

DUODENUM DIVERTICULA

smaller than those during life because of some shrinkage due to the embalming process; nevertheless, it is believed that the difference is of no practical importance.

Before roentgenologic examination became available, and made early recognition of this interesting lesion possible, during a period of 212 years (1710-1912), less than 100 cases were reported, and they were of only academic interest. They were found at necropsies exclusively.

How little attention they received in those days is evident from Cruveilhier's report in 1849. When writing on diverticula of the gastro-intestinal tract, he described pouches in the esophagus and colon, and stated that diverticula did not occur between these points.

From the moment when Case first diagnosed a duodenal diverticulum roentgenographically, in 1913, the number of reported cases commenced to increase rapidly, and, in 1932, Lockwood was able to cite a grand total of 357 cases diagnosed roentgenologically.

This total compared with the one recorded for the preroentgenographic period is high, and especially so when taking into consideration the great difference in the length of the two respective periods. Relatively speaking, however, no actual increase of duodenal diverticula was observed.

That this is true can be seen when roentgenologic figures are compared with the figures obtained at necropsies and both are expressed in percentages, as demonstrated in Table I. Indeed, a much higher frequency is observed in autopsy reports.

TABLE I
PERCENTAGE-FREQUENCY OF DUODENAL DIVERTICULA FOUND AT AUTOPSIES AND AT ROENTGENOLOGIC EXAMINATIONS

Author	Year	Number of Autopsies	Number of x-ray Examinations	Duodena with Diverticula	Percentage
Schuppel	1880	45		7	15.5
Rosenthal	1908	100		3	3
Baldwin	1911	105		14	13.3
Linsmayer	1914	1367		45	3.3
Horton & Mueller	1933	216		11	5.09
Grant	1920	133		15	11.3
Case	1921		6847	85	1.2
Andrews	1926		2200	26	1.18
Spriggs & Marxer	1927		1000	38	3.8
Cryderman	1934		770	40	5.19
Lemmel	1934		3324	50	1.5
Rankin & Martin	1934		72715	111	0.016
Edwards	1939		11362	85	0.75

Thus, Maclean may be right in suggesting that roentgenograms are only efficient in diagnosing a minority of diverticula. In that event they might lead to erroneous conceptions as to the incidence of these pouches as well as to their clinical importance, particularly so, because a definite diagnosis depends exclusively on the roentgenologic findings. These are not infrequently misinterpreted, and actual diverticula are diagnosed as calcified nodes, gallstones, renal calculi, fecaliths, pancreatic calcifications, ulcer craters, redundancies, and traction pouches due to adhesions.

FIG. 9.



FIG. 10.

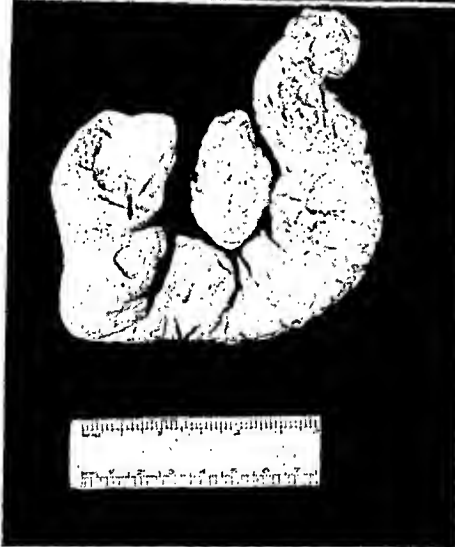
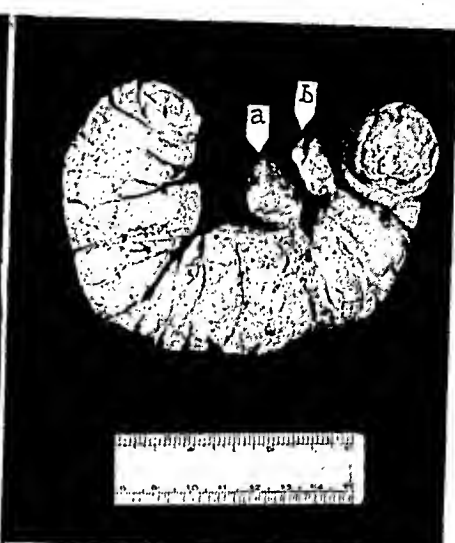


FIG. 11.

FIG. 12.

FIG. 9.—A very narrow orifice leads to a fairly large diverticulum of the third part. The arrow indicates the site of the papilla.

FIG. 10.—There are two diverticula, *a* in the third, and *b* in the fourth part of the duodenum. Both have narrow orifices.

FIG. 11.—A large oblong-shaped diverticulum of the fourth part shows a very short and narrow orifice.

FIG. 12.—The cast is of a duodenum which was composed of the first three parts only. The arrow indicates the location of the papilla.

DUODENUM DIVERTICULA

It is quite obvious that duodenal diverticula may not always be visualized, because the barium either is expelled too rapidly or it fails to fill the pouch. Scott is of the opinion that fluoroscopic palpation is of primary importance in diagnosing diverticula, and believes that unless the barium is dammed up and manipulated into the pouch with the hands on the abdomen, little or none of the meal may enter. Heacock strongly recommends the use of a duodenal tube for filling the duodenum with barium. This is especially advisable in doubtful cases according to McKinney. Diverticula may also not always be recognized, and Costello stresses the inadequacy of the usual roentgenographic examination. He reports that in four of his six cases the diverticula were not observed until after more than one barium meal. The stomach and first part of the duodenum takes up so much of the examiner's attention, he continues, that the second, third and fourth parts of the duodenum may be neglected.

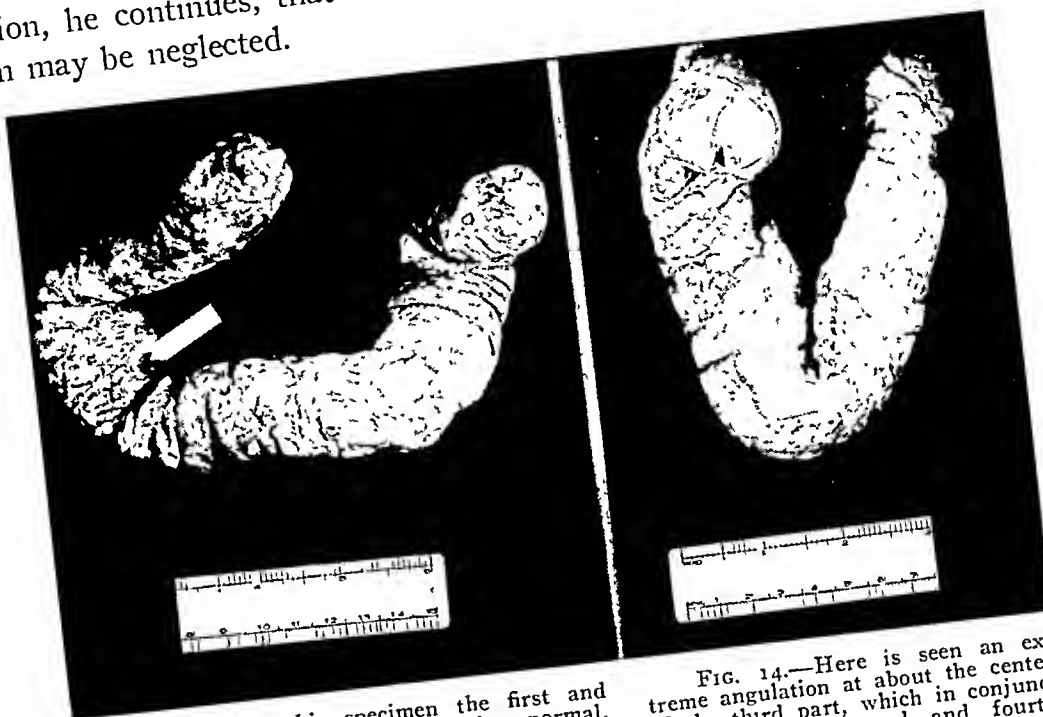


FIG. 13.—In this specimen the first and third parts are considerably larger than normal, while the second and fourth parts are quite short in proportion. Arrow indicates the location of the papilla.

FIG. 14.—Here is seen an extreme angulation at about the center of the third part, which in conjunction with the second and fourth parts give the duodenum the shape of the letter V.

Friedlander believes that serial exposures taken during screen examinations are very helpful for fixing the findings which disappear very quickly. In his opinion supine and prone positions with some rotation to the right and left and sometimes a semi-Trendelenburg position should be used, as some diverticula fill better in this way.

There may be other complicating factors as, for example, the stomach when hanging down obscures the presence of diverticula in the third part of the duodenum, or as Case points out, diverticula in the third part fail to retain barium unless the communicating orifice is small.

In spite of numerous technical difficulties encountered in diagnosing diverticula roentgenologically, a comprehensive review of the literature on the subject disclosed that these anomalies have been found quite frequently.

However, one is led to the conclusion that in most cases they have not been considered the cause of any symptoms. The validity of such an assumption can be judged from the fact that, although the condition has been known to the medical profession since 1710, when Chomel first reported such a case, no clean-cut picture has been described, by which a clinical diagnosis could be established.

There is no symptom-complex characteristic of a duodenal diverticulum, but there are a number of symptoms associated with it, and Spriggs and Marxer believe that such an association has either not been recognized, or has received but little attention, and that diverticulosis is much more common than has been hitherto recognized. Scott is of a similar opinion, and Lockwood and Maclean consider duodenal diverticula to be a clinical entity. Rankin and Martin state that in unexplained abdominal complaints diverticulosis must be thought of and ruled out.

It is evident from numerous reports that cases of such maladies most frequently are interpreted clinically as appendicitis, cholecystitis, pancreatitis, duodenitis, and gastric or duodenal ulcers, because diverticula may become inflamed or undergo other pathologic changes; they may become gangrenous and perforate or even cause obstructions, not only of the duodenum, but also of the common bile duct and the pancreatic duct as well.

The only case in which a primary carcinoma has occurred in association with a duodenal diverticulum was reported by Morrison and Feldman (1926).

Incidentally, this study of the duodenum by means of casts disclosed some of its less widely known anatomic variations, and the following observations were made:

A. The papilla of Vater in this series, as indicated by Figures 3, 7, 8, 9, 12 and 13, was found to be situated at the lower bend of the descending portion of the duodenum, at the medial side and at the posteromedial side as well (not seen in these front-view illustrations). Gray places it a little below the middle of the descending portion and at the medial side. Piersol and Cunningham locate it $3\frac{1}{2}$ –4 inches, and Grant 7.9 cm. beyond the pylorus. How much reliance can be placed, without reservation, upon such figures may be clearly seen when the distance from the pylorus to the papilla is compared in Figures 8 and 9.

B. That shapes, too, may vary considerably, a fact seen particularly in Figures 13 and 14.

C. That not all duodena consist of four parts; either the fourth portion is absent, as in Figure 12, or the third and fourth parts are represented by one portion ascending obliquely as in Figures 1 and 6. Some of these are angulated to such an extent that, in conjunction with the second part, they have the shape of the letter V, as in Figure 14.

CONCLUSIONS

1. This series would seem to indicate that duodenal diverticula are more common than has hitherto been believed.

DUODENUM DIVERTICULA

2. Neither roentgenologic nor anatomic figures are conclusive regarding the actual incidence of diverticula of the duodenum.
3. It is obvious that the important points in roentgenologic diagnosis of duodenal diverticula are both a perfect technic and a genuine interest by the roengenologist in the particular subject.
4. A new method by which even the most obscure diverticula are revealed is described.
5. The papilla of Vater is not constant as to its location.
6. The duodenum is not infrequently made up of three parts instead of the classical four, and it may also vary as to its configuration and size.

The writer wishes to express his appreciation of the assistance given by Dr. J. W. Jobling, of the Department of Pathology, and particularly by Dr. D. J. Morton, of the Department of Anatomy, in connection with this paper.

He is especially indebted to Dr. Allen O. Whipple for his interest, his helpful advice and constructive suggestions, as well as for his permission to examine all bodies used in his lectures on Surgical Anatomy over a period of three years.

REFERENCES

- 1 Akerlund, Ake: Fortschr, a.d. Geb. d. Roentgenstrahlen, 25, 540, 1917.
- 2 Alesen, L. A.: M. Rec., 149, 261, 1939.
- 3 Andrews, E. W.: J. A. M. A., 77, 1309, 1921.
- 4 Armstrong, J. R.: Brit. Med. Jour., 1, 1230, 1939.
- 5 Avancini, von. L. P.: Deutsche Ztschr. f. Chir., 252, 529, 1939.
- 6 Bainbridge, W.: Texas State M. J., 22, 560, 1927.
- 7 Baldwin, W. M.: Anat. Rec., 5, 121, 1911.
- 8 Basch, S.: Am. J. M. Sc., 153, 833, 1917.
- 9 Bassett, V. H.: Tr. Chicago Path. Soc., 7, 83, 1907.
- 10 Bauer, Theodor: Wien. klin. Wochnschr., 25, 879, 1912.
- 11 Beals, J. A.: South, M. J., 30, 218, 1937.
- 12 Beaver, J. L.: ANNALS OF SURGERY, 108, 153, 1938.
- 13 Bell, Howard H.: Anat. Record, 21, 229, 1921.
- 14 Bengolea, A. J.: Bull. et Mem. Soc. nat. de Chir., 54, 726, 1928.
- 15 Boland, F. K., Jr.: Surgery, 6, 65, 1939.
- 16 Buckstein, J.: Am. J. Surg., 3, 340, 1927.
- 17 Buschi, Guiseppe: Virchows Arch. f. path. Anat., 206, 121, 1911.
- 18 Carson, H. W.: Tr. Med. Soc. Lond., 53, 76, 1930.
- 19 Case, J. T.: Am. J. Roentgenol., 3, 314, 1916.
- 20 Case, J. T.: J. A. M. A., 75, 1463, 1920.
- 21 Chomel, J. B. L.: Histoire de L'Academie Royale. Paris, 1710.
- 22 Cole, L. G., and Roberts, Dudley: Surg., Gynec. & Obst., 31, 376, 1920.
- 23 Costello, C. D.: Brit. J. Radiology, 6, 577, 1933.
- 24 Cronie, D.: Brit. M. J., 2, 1021, 1933.
- 25 Cryderman, W. J.: Canad. Med. Assoc. J., 17, 1455, 1927.
- 26 Cullen, E. K.: Arch. Surg., 2, 542, 1921.
- 27 Davis, N. S.: Tr. Chicago Path. Soc., 9, 1, 1913.
- 28 Downes, W. A.: ANNALS OF SURGERY, 76, 43, 1922.
- 29 Edwards, H. C.: Surg., Gynec. & Obst., 60, 946, 1935.
- 30 Edwards, H. C.: Diverticula and Diverticulitis of the Intestine. Bristol, John Wright & Sons, Ltd., 1939.
- 31 Falconer, A. W.: Lancet, 1, 1296, 1907.
- 32 Finsterer, H.: Med. Klinik, 32, 243, 1936.

- 33 Fischer, M. H.: *J. Exper. Med.*, 5, 333, 1900.
- 34 Fleischmann, Gottfried: *Leichen Oeffnungen*, 16, 264 pp., Erlangen, 1815.
- 35 Fletcher, H. N., and Castleden, L. I. M.: *Brit. J. Surg.*, 23, 776, 1936.
- 36 Forssell, Gösta, and Key, Einar: *Nord. med. Arkiv*, 48, 15, 1915.
- 37 Friedlander, G.: *Brit. J. Radiol.*, 10, 26, 1937.
- 38 Gibbon, W. H.: *Radiology*, 21, 491, 1933.
- 39 Glickman, L. G.: *Radiology*, 23, 479, 1934.
- 40 Grant, J. C. B.: *Jour. Anat.*, 57, 357, 1922-3.
- 41 Grant, J. C. B.: *Canad. Med. Assoc. Jour.*, 33, 258, 1935.
- 42 Habershon, S. O.: *Observation on Diseases of the Alimentary Canal*, 1857.
- 43 Hahn, O.: *Klin. Wchnsehr.*, 9, 1922-1925, October 11, 1930.
- 44 Harley, G.: *Tr. Path. Soc. Lond.*, 8, 235, 1857.
- 45 Heacock, C. H.: *South. Med. Jour.*, 22, 348, 1929.
- 46 Herbst, W. P.: *Minnesota Med.*, 10, 364, 1927.
- 47 Hodenpyl, E.: *Tr. New York Path. Soc.*, 1901.
- 48 Horton, B. T., and Mueller, S. C.: *Arch. Surg.*, 26, 1010, 1933.
- 49 Huddy, G. P. B.: *The Lancet*, 2, 327, 1923.
- 50 Jaecuelin, C., and Quenu, J., Jr.: *Bull. et Mem. Soc. nat. de Chir.*, 53, 716, 1927
- 51 Kaldor, J.: *ANNALS OF SURGERY*, 89, 6, 1929.
- 52 Keith, Sir Arthur: *Brit. Med. J.*, 1, 376, 1910.
- 53 King, M. K.: *South. M. J.*, 26, 869, 1933.
- 54 Larimore, J. W., and Graham, E. A.: *Surg., Gynec. & Obst.*, 45, 257, 1927.
- 55 Letulle, Maurice: *Bull. Soc. Anat. de Paris*, 1898.
- 56 Lemmel, G.: *Arch. f. Verdaungskr.*, 56, 59, 1934.
- 57 Lewis, Dean: *J. A. M. A.*, 76, 783, 1921.
- 58 Lewis, F. T., and Thyng, F. W.: *Amer. J. Anat.*, 7, 505, 1908.
- 59 Linsmayer, Heinrich: *Verhandl. d. deutsch. path. Gesellschaft*, 17, 445, 1914.
- 60 Lockhart, R. H.: *Yale J. Biol. Med.*, 3, 505, 1931.
- 61 Lockwood, A. L.: *J. A. M. A.*, 98, 961, 1932.
- 62 Lucinian, J. H.: *Am. J. Roentgenol.*, 24, 684, 1930.
- 63 Lund, F. B.: *New England, M. J.*, 198, 986, 1928.
- 64 MacGuire, D. P.: *Intern. J. Med. & Surg.*, 48, 153, 1935.
- 65 Mackechnie, H. N.: *ANNALS OF SURGERY*, 74, 96, 1921.
- 66 Maclean, N. J.: *Surg., Gynec. & Obst.*, 37, 6, 1923.
- 67 Maclean, N. J.: *ANNALS OF SURGERY*, 85, 73, 1927.
- 68 Marie, M. R.: *Bull. Soc. Anat.*, 74, 982, 1899.
- 69 McKinney, J. T.: *South. Med. Jour.*, 24, 753, 1931.
- 70 McQuay, R. W.: *ANNALS OF SURGERY*, 89, 36, 1929.
- 71 Mendillo, H. J., and Koufman, W. B.: *New England, J. Med.*, 219, 432, 1938.
- 72 Molesworth, H. W. L.: *Brit. Jour. Surg.*, 17, 342, 1929.
- 73 Monsarrat, K. W.: *Brit. Jour. Surg.*, 14, 179, 1926.
- 74 Moore, E. C.: *Arch. Surg.*, 1, 513, 1920.
- 75 Morgagni, G. B.: *DeSedibus et Causis Morborum*, Naples, 1762.
- 76 Morrison, T. H., and Feldman, M.: *Tr. Am. Gastro-Enterol. Assn.*, 29, 271, 1926.
- 77 Morton, J. J.: *Surgery*, 8, 265, 1940.
- 78 Nagel, H. W.: *Arch. Surg.*, 2, 529, 1925.
- 79 Nicholson, W. M.: *Bull. Johns Hopkins Hosp.*, 56, 305, 1935.
- 80 Odgers, P. N. B.: *Brit. J. Surg.*, 17, 592, 1930.
- 81 Ogilvie, R. F.: *Brit. J. Surg.*, 28, 362, 1941.
- 82 Pendergrass, R. C.: *Radiology*, 17, 1216, 1931.
- 83 Perry, E. C., and Shaw, L. E.: *Guy's Hospital Rep.*, 50, 171, 1893.
- 84 Pilcher, L. S.: *ANNALS OF SURGERY*, 2, 62, 1894.
- 85 Rankin, F. W., and Brown, P. W.: *Surg., Gynec. & Obst.*, 50, 836, 1930.

DUODENUM DIVERTICULA

Volume 117
Number 3

- 86 Rankin, F. W., and Martin, W. J., Jr.: *ANNALS OF SURGERY*, 100, 1123, 1934.
- 87 Rich, A. R., and Duff, G. L.: *Johns Hopkins Hosp.*, 58, 212, 1936.
- 88 Ritchie, H. P., and McWhorter, G. L.: *Surg., Gynec. & Obst.*, 25, 485, 1917.
- 89 Rokitansky, Carl: *Lehrbuch der pathologischen Anatomie*, Vienna, 1861.
- 90 Rosenthal, Th.: *Med. Klin.*, 4, Bd. 2, 1421, 1908.
- 91 Roth, M.: *Virchows Arch. f. path. Anat.*, 56, 197, 1872.
- 92 Schüppel von, O.: *Die Krankheiten der Gallenwege und der Pfortader*. In: *Handbuch der speziellen Pathologie und Therapie*, 8, 1, Hälfte, 2. Abth., Div., p. 228, 1880.
- 93 Scott, S. G.: *Brit. M. J.*, 1, 346, 1931.
- 94 Seippel, O.: *Zurich*, 1895.
- 95 Spriggs, E. T., and Marxer, O. A.: *Brit. Med. J.*, 1, 130, 1926.
- 96 Tandler, Julius: *Morphol. Jahrb.*, 29, 187, Leipzig, 1902.
- 97 Tanner, W. E.: *Lancet*, 2, 853, 1936.
- 98 Thorek, M.: *Illinois Med. J.*, 55, 64, 1929.
- 99 Turner, F. C.: *Tr. Path. Soc. Lond.*, 35, 200, 1884.
- 100 Turner, G. Grey: *Lancet*, 1, 151, 1920.
- 101 Versmann, G. N.: *Beitr. z. klin. Chir.*, 118, 735, 1920.
- 102 Weiss, K.: *Frankfurt, Ztschr. f. Path.*, 1929.
- 103 Wheeler, D.: *Canad. Med. Assoc. J.*, 39, 241, 1938.
- 104 Wilkie, D. P. D.: *Edinburgh M. J.*, 11, 219, 1913.

GASTROJEJUNOCOLIC FISTULAE: WITH SPECIAL REFERENCE TO ASSOCIATED NUTRITIONAL DEFICIENCIES AND CERTAIN SURGICAL ASPECTS

JOHN S. ATWATER, M.D.,

FELLOW IN MEDICINE, MAYO FOUNDATION

Lt. HUGH R. BUTT, MC-V (S) U.S.N.R.,*

AND

JAMES T. PRIESTLEY, M.D.,

DIVISION OF SURGERY, MAYO CLINIC

ROCHESTER, MINN.

FEW DISEASE SYNDROMES are capable of producing such a diversity of nutritional deficiencies so rapidly as the syndrome which may accompany gastrocolic or gastrojejunocolic fistula. For many years the deficient nutritional status of patients who have this condition has been one of the largest contributing factors to the high mortality rate attendant on the surgical treatment of this lesion. In the past, at least part of the high surgical mortality rate in such cases could be attributed to inadequate medical treatment, both preoperatively and postoperatively. But in view of the present knowledge of nutrition, these inadequacies should be overcome and the added surgical risk entailed by nutritional deficiencies should be largely eliminated.

A series of patients who had gastrojejunocolic fistula was studied with a twofold purpose: First, for review of the clinical observations and determination of the incidence, predisposing factors, signs, symptoms and the ultimate outcome of patients who have gastrocolic fistulae; second, for consideration of the clinical evidence of associated metabolic deficiency diseases. In focusing attention on the poor nutritional status of these patients, we hope that the need for adequate preoperative and postoperative care will be emphasized in the achievement of the best surgical results.

The material presented herein was selected from the records of the Mayo Clinic in the seven-year period from January, 1935, to January, 1942. Forty-two patients who had surgically-proved gastrocolic or gastrojejunocolic fistulae were encountered during this period. In 40 of these 42 cases the fistulae were associated with benign disease, and in the other two, complicated malignant disease of the upper portion of the gastro-intestinal tract was associated. Certain of these cases were included in a series reported previously by Gray and Sharpe.¹

Gastrocolic or gastrojejunocolic fistulae may be the sequelae of three different types of disease process: First, there are those which complicate cancer of the stomach or colon; second, those which complicate gastrojejunal ulcers; and third, those associated with miscellaneous diseases, such as abscess in the peritoneal cavity, visceral tuberculosis, syphilis, trauma, and

* On leave from Division of Medicine, Mayo Clinic.

GASTROJEJUNOCOLIC FISTULA

possibly congenital deformities² of the gastro-intestinal tract. Those which complicate gastrojejunal ulcers are, by far, the most common.

HISTORICAL ASPECTS

Gastrocolic Fistula and Cancer.—Haller,³ in 1755, made the first report of a case in which gastrocolic fistula complicated a malignant process of the stomach. Zweig⁴ had collected 70 cases of this type by the turn of this century, and, in 1940, Thomas² reported or mentioned a total of 141 cases. Since in this group gastrocolic fistula generally occurs only after the malignant disease is far advanced, and since modern diagnostic methods make possible the earlier recognition of the underlying cancer in most cases, fewer and fewer cases of this type have been reported.

Postgastrojejunal Ulcer Group.—Wolfer⁵ performed the first anterior type of gastro-enterostomy in 1881, and von Hacker⁶ performed the first posterior type of gastro-enterostomy in 1885. Four years later (in 1889), Braun⁷ made the first report of a gastrojejunal ulcer, and, in 1903, Czerny⁸ made the first report of a case in which gastrojejunocolic fistula followed gastrojejunal ulcer. By 1940, Thomas had collected references to 207 cases in which gastrocolic or gastrojejunocolic fistula had followed gastrojejunal ulcer.

INCIDENCE

Thus, until the advent of gastric surgery for the treatment of duodenal ulcer, most gastrocolic fistulae were associated with cancer of the stomach and colon. As gastro-enterostomy began to be performed frequently, the incidence of gastrocolic and gastrojejunocolic fistula increased proportionately to the number of gastrojejunal ulcers which developed. Probably because of anatomic reasons, fistulae of this type seldom occur after the performance of anterior gastro-enterostomy. It is also of interest to notice that after posterior gastro-enterostomy has been performed for gastric ulcer, gastrojejunocolic fistula develops infrequently, as do gastrojejunal ulcers.

Reports of the incidence of gastrojejunal ulcer which occurs after gastro-enterostomy vary widely. Lahey⁹ stated that an incidence of 15 per cent ascribed to the condition would be fairly accurate. However, in various reports, such as those by Walton,¹⁰ from the London Hospital, Allen,¹¹ from the Massachusetts General Hospital, and Walters and Clagett,¹² from the Mayo Clinic, agreed that the incidence is about three to four per cent. In arriving at such an incidence, the latter authors assumed that in the several series, on which they based their conclusions, the operation of gastro-enterostomy had been properly selected for the individual patient and correctly performed.

The incidence of gastrojejunal ulcer occurring after gastric resection, when that operation has been considered properly the operation of choice for a given patient with duodenal ulcer, and when it has been performed in an approved manner, is lower than it is after gastro-enterostomy. Likewise, the incidence of gastrojejunocolic fistula after gastric resection is lower

under these circumstances. The incidence of gastrojejunal fistula in the presence of gastrojejunal ulcer has been reported to be from 11 to 14 per cent. Walters and Clagett reported this incidence to be 13.6 per cent. Allen has reported it to be 14 per cent.

FACTORS OF AGE AND SEX

Lahey and Swinton¹³ stated that gastrojejunal fistulae usually occur among patients from 30 to 45 years old. In Rife's¹⁴ series the average age of the patients was 46 years. In Walters and Clagett's series the age group was from 40 to 60 years. In the present series the average age of the patients at the clinical onset of gastrocolic or gastrojejunal fistula, excluding two cases in which the condition was secondary to malignant disease, was approximately 45 years. The two patients who also had cancer were 65 and 72 years old, respectively. Of the remaining 40 patients, the youngest was 28 years old and the oldest was 68 years old. From this point onward, only the 40 patients whose background condition was benign will be considered herein, and the two patients just mentioned, in whom fistulae developed secondary to carcinoma, will be omitted.

It is difficult to state the incidence of duodenal ulcer among men and women. However, Robertson and Hargis¹⁵ in a pathologico-anatomic survey of duodenal ulcers found evidence of healed or active ulcers in 11.8 per cent of cases. Their observations were based on results of necropsy as performed 2,000 times. Certain clinical roentgenologic studies support their conclusion, for in one 12-month period at the Mayo Clinic duodenal ulcers were found in 12 per cent of the 16,000 gastroduodenal examinations performed during that period.¹⁶ Balfour and Eusterman stated that peptic ulcer occurs four times more often among men than among women; that gastrojejunal ulcer occurs seven times more often among men than among women, and that gastrojejunal fistula almost never occurs among women.

In this series proper, there were no cases in which gastrocolic or gastrojejunal fistula had occurred among women. In all the 40 cases the fistulae had developed among men as sequelae to gastrojejunal ulcers. The two patients who had fistulae which complicated a malignant process were women.

FACTOR OF PREVIOUS OPERATIONS

In all instances the fistulae followed some surgical procedure on the upper part of the gastro-intestinal tract. In 23 cases (58 per cent) the fistulae followed posterior gastro-enterostomy; in 14 cases (35 per cent) the fistulae followed an unidentified type of gastro-enterostomy. Gastrectomy preceded one instance of fistula, and an unidentified type of operation preceded still another instance. In no case was a fistula preceded by performance of an anterior type of gastro-enterostomy. This brief summary brings the total number of cases to 39.

In the fortieth case there had been a previous surgically-proved gastro-

jejunocolic fistula. The patient in this case was of especial interest. After 15 years of typical symptoms and roentgenologic evidence of a duodenal ulcer, the ulcer perforated. The perforation was closed and a posterior type of gastro-enterostomy was performed. Four years later symptoms of a gastro-jejunal ulcer were noticed. This ulcer, in turn, after another interim of six years, gave rise to a gastrojejunocolic fistula. At operation, the posterior gastro-enteric anastomosis was disestablished, the fistula was excised, and the openings in the jejunum and stomach were closed. That portion of the colon containing the fistulous opening was exteriorized, as is done in performance of a Mikulicz operation. Soon thereafter the old duodenal ulcer became reactivated and perforated acutely. Simple closure of the perforated ulcer was performed. The ulcer remained active, symptoms of pyloric obstruction developed and, at the end of eight months, a posterior type of gastro-enterostomy was performed because there was such a large inflammatory mass surrounding the duodenal ulcer that gastric resection could not be accomplished. After this operation the patient complained of unmistakable symptoms of gastrojejunal ulcer and a gastrojejunocolic fistula soon developed for the second time. Operation was again performed and the fistula was excised, but the patient succumbed on the sixth postoperative day, from pneumonia.

INTERIM BETWEEN INITIAL OPERATION AND ONSET OF SYMPTOMS OF GASTROJEJUNOCOLIC FISTULA

It is interesting to observe the interval that elapsed between the initial operative procedure and the onset of symptoms attributable to gastrojejunocolic fistula. In 17 cases a fistula developed within a year after operation; in 24 cases a fistula developed within two years after operation; in 27 cases a fistula had developed by the third year after operation; in 28 cases a fistula had developed by the fifth year after operation; and in 35* cases a fistula had developed by the end of the tenth year after operation. In the remaining five cases a fistula occurred between 10 and 20 years after the original operations (Table I).

TABLE I
INTERIM BETWEEN OPERATION AND ONSET OF SYMPTOMS IN
40 PATIENTS WHO HAD GASTROJEJUNOCOLIC FISTULAE

Years Since Operation	No. of Cases in Each Period	Cumulative No. of Cases in Each Period
0 to 5	28	28
6 to 10	7	35
11 to 15	2	37
16 to 20	3	40

SIGNS AND SYMPTOMS

Diarrhea.—Diarrhea was present in 39 of the 40 cases. Often diarrhea was the presenting complaint, and it was of a varying degree of severity. In 27 cases diarrhea was intermittent in character or moderately severe—

* Each number, of course, includes the total in the group which immediately precedes it.

meaning that 6 to 12 stools were passed daily. In the remaining cases passage of stools occurred more frequently.

The stools were described as being either "loose and watery" or "mushy and infantile" in form and consistency. They were often copious and the color usually was described as "light yellow" or "gray-white." In some instances they were described as "foamy," "greasy" and "able to float on water." It is noteworthy that the stools rarely were bloody. In 28 per cent of cases the stools contained abnormal quantities of undigested food particles. In certain cases undigested food from the patient's previous meal was recognized in the stools within from two to four hours after eating. Thirty-five per cent of the patients had stools which contained an abnormal amount of fat. In a few instances determination was made of the percentage of fat in the stools, and in each case an increased quantity of fat was reported. Approximately a fourth of the patients complained of the necessity of the nocturnal passage of multiple stools.

Some effort was made to correlate the size of the ostia of the fistulous tract with the severity of the diarrhea. In general, those patients in whom the diameter of the ostia was less than two centimeters had more intermittent and milder diarrhea than those patients in whom the diameter of the ostia was larger than two centimeters.

Loss of Weight.—In general, loss of weight was directly proportional to several factors; namely, duration of the disease, severity of the diarrhea and, in turn, the relative diameter of the ostia of the fistulous tract. An occasional patient exhibited no change in weight, but others lost as much as 50 pounds (23 Kg.) within five or six months after the development of the gastrojejuncocolic fistula.

Loss of Strength.—Loss of strength was severe in a few cases, moderate in most cases, and absent in only five per cent of cases (Table II). Seventy-eight per cent of the patients had moderately severe loss of strength. Dehydration was frequent and paralleled the severity of the diarrhea and the loss of strength and weight.

TABLE II
GENERAL AND MISCELLANEOUS DEFICIENCIES OBSERVED IN 40 PATIENTS
WHO HAD GASTROJEJUNOCOLIC FISTULAE

	Number of Observations
Emaciation and dehydration.....	23
Nutritional edema.....	10
Ascites.....	1
Loss of strength.....	38
Loss of weight.....	31
Disease of liver	
Value for serum protein reduced*.....	15
Fatty liver (observed at operation or at postmortem).....	7
Dye retention (Grade 2).....	1
Definitely low albumin-globulin ratio.....	3
Low normals.....	6
Salt craving.....	1
Loss of body hair.....	1

*Eighty-eight per cent of patients tested had definitely lowered values for protein in the serum; lowest value was 3.7 Gm., and average value was 4.9 Gm. per 100 cc.

Stercoraceous Eructation and Vomiting.—Another prominent complaint was belching or vomiting of material which the patient said tasted like, and which often appeared to be, fecal substance. Approximately half of the patients complained of fecal belching, 38 per cent complained of fecal vomiting and 30 per cent gave no history of either. There were two cases in which vomiting of material not fecal in character occurred. In many instances the test meal produced material similar to feces in odor and color. In view of the nature of the gastric contents, values for hydrochloric acid as noted in analysis of a test meal were thought to be of little significance.

EVIDENCE OF NUTRITIONAL DEFICIENCIES

Gastrojejunal fistula causes a disease syndrome in which there is a unique pathologic anatomic situation especially conducive to the development of nutritional deficiencies. Other diseases, such as chronic ulcerative colitis, sprue, celiac disease and the chronic diarrheas, are capable of producing similar states of nutritional deficiency. In the case of gastrojejunal fistula, however, the mechanical factor, rather than any disease process, is foremost. When gastrojejunal fistula is present, food taken orally actually spends little time in the gastro-intestinal tract. It is shunted out of the stomach and into that portion of the bowel in which it is known that only little absorption of food takes place. In fact, the total time which orally ingested food spends in the entire gastro-intestinal tract may be as short as from one to two hours. Fluids, also, have but little time for absorption by the gastro-intestinal tract, and as a result most stools are loose and liquid.

In the presence of gastrojejunal fistula, in addition to the rapid passage of gastric contents through the alimentary tract, as just described, there is a decrease in the available absorptive intestinal surface with which food comes into contact. Some nutriment is obtained, but most of the food and fluid passes on largely unchanged, except by mastication. This is recognized readily by the presence of abnormally high quantities of food fats and undigested food particles in the watery stools. The disturbance in water balance is manifest by the prominent dehydration which most patients display.

When gastrojejunal fistula has occurred there is ample clinical evidence of inadequate provision of the important foodstuffs, namely carbohydrates, proteins, fats and vitamins. Undernutrition generally is outstanding. Mention has been made of the striking losses in weight and strength encountered. Twenty-three patients (58 per cent) exhibited a marked degree of emaciation and dehydration (Table II).

It is well known that deprivation of proteins provokes hypoproteinemia and that this, in turn, may induce changes productive of shifts in body fluids. Edema interpreted as being "nutritional" in origin was present among ten patients (25 per cent) and one of these patients had associated ascites which could be explained on no other basis. The value for proteins in the serum was estimated among a number of patients, and in almost every instance it was found to be low. Values for protein in the serum varied

from the low figure of 3.7 to 4.9 Gm. per 100 cc. In some cases values for both albumin and globulin were lowered. Tests of hepatic function were not performed regularly; however, in seven cases the surgeon at the time of operation or the pathologist at the time of necropsy was impressed sufficiently to remark on the fatty condition of the liver.

Deficiency of iron in the body will produce a hypochromic form of anemia; a deficiency of Castle's antianemic principle will produce a macrocytic form of anemia. Such was found to be true in this study. Examination of the blood revealed definite changes in many cases. The lowest erythrocyte count was 3,363,000, and the lowest value for hemoglobin was 8.4 Gm. per 100 cc. In 68 per cent of cases the erythrocyte count was less than 4,500,000 and in 15 per cent of cases it was less than 4,000,000. In 52 per cent of cases the value for hemoglobin was below the normal range. Examination of blood smears disclosed macrocytosis to be present in 14 per cent of cases.

When the manifold evidence of general undernutrition was considered; that is, loss of weight and of strength, dehydration and emaciation, peripheral edema, ascites, hypoproteinemia and anemia, it seemed probable that certain vitamin deficiencies should find clinical expression. Such was the case. These patients had been observed during a period in which refined laboratory measurements of vitamin deficiency diseases were being developed. With few exceptions, evidence of avitaminosis had to be adduced from the clinical observations alone. The guideposts for the clinical recognition of vitamin deficiency states were many. A solitary deficiency state seldom existed. The number of instances of vitamin deficiency observed was in direct proportion to the severity of the diarrhea and the duration of the disease.

Patients who have chronic diarrhea are known to have a greater requirement for vitamins than normal persons have.¹⁷ The decrease in the power of adaptation to dark is one of the earliest manifestations of vitamin A deficiency. Two patients displayed a marked degree of this, as nyctalopia or "night blindness" (Table III). At the time of observation the test for adaptation to dark was not used clinically as widely as it is now, so that the exact degree of dysadaptation to dark was not observed.

Absence of members of the vitamin B-complex provoked the most striking evidence of vitamin deficiency states. A third of the vitamin deficiencies observed were in this category. Lack of the thermolabile antineuritic component, thiamine, was disclosed by the presence of burning, superficial paresthesias, and in one instance severe peripheral neuritis was noted. The patient who complained of the latter condition also had a typical type of niacin deficiency, pellagra. The cutaneous lesions were characteristic. Glossitis was observed twice, and was ascribed to a lack of either niacin or riboflavin. Closely related was the occurrence of cheilosis in three patients; in one of them a noninfectious type of conjunctivitis was noted. These were considered to be typical instances of B-complex deficiency, and in the light of present knowledge could be attributed to a deficiency of riboflavin.

GASTROJEJUNOCOLIC FISTULA

TABLE III
TYPES OF VITAMIN DEFICIENCY OBSERVED AND SYMPTOMS THEREOF IN 40 PATIENTS
WHO HAD GASTROJEJUNOCOLIC FISTULAE

Deficiency and Symptoms of	No. Having Symptoms
Vitamin A:	
Nyctalopia	2
Thiamine:	
Paresthesias	1
Peripheral neuritis	1
Riboflavin:	
Cheilosis	3
Glossitis	2
Conjunctivitis	1
Niacin:	
Pellagra	1
Ascorbic acid:	
Lowered values in blood*	11
Ecchymoses	1
Vitamin D:	
Tetany (carpopedal spasm)	1
Vitamin K:	
Prolonged Quick prothrombin time	6
Total	30

*These 11 patients were all that had been tested for this acid. In all 11 the values were lower than normal.

Both clinical and laboratory observations were used to detect vitamin C deficiency. Eleven patients had been tested for values for ascorbic acid in the blood. All had definitely lowered values for this acid. One patient in this group had multiple ecchymoses.

Quick prothrombin times had been determined in 14 cases, and in this group a definitely prolonged time was present in 43 per cent. One patient had a Quick prothrombin value of 90 seconds as compared with a normal time of 20 seconds. This case was one of particular interest, being one in which the condition was most severe, the patient displaying pellagrous lesions, carpopedal spasm and other evidences of nutritional disturbances.

Preoperative Preparation.—Inasmuch as a large proportion of patients who have gastrojejunocolic fistula exhibit clinical evidence of marked deficiency disease, it is obvious that a most energetic effort to restore the patient to proper physical and chemical health prior to operation should be considered of utmost importance. Such an effort can be made by means of good preoperative care. Treatment of this type also should be continued postoperatively. There is no specified textbook procedure. The primary objective is to restore the patient to good nutritional balance as quickly and as economically as possible. Gray and Sharpe reported a mortality rate of 61.5 per cent in a series of cases in which operation had been performed for gastrojejunocolic fistula without adequate preoperative preparation of the patients, in contrast with a mortality rate of 27.7 per cent in a group of patients who received adequate preoperative care.

Adequate quantities of fluids in the form of physiologic solution of sodium chloride and solutions of glucose should be given by hypodermoclysis. Transfused blood and plasma are of value. In addition to the fact that they con-

tribute a certain amount of fluid, the former are valuable in that they tend to restore protein to the plasma. The use of extracts of iron and liver may be indicated. A high caloric, high vitamin and low residue diet is suggested.

No elaborate plan of dosage of vitamins is necessary so long as the amounts administered are in excess of the optimal standards as adopted by the National Research Council¹⁸ for an active person. Preparation should be carried on not for one day preoperatively, but should extend over a longer period. In general, the preoperative program should be planned so as to replenish generously each of the sorely depleted nutritional stores of the body, and as a rule requires one week to two weeks.

SURGICAL ASPECTS

Many different surgical procedures have been suggested for the treatment of gastrojejunocolic fistula. As experience with the surgical management of this lesion has increased, the relative appreciation of the advantages and disadvantages of the various procedures has become more nearly accurate. Some surgeons have endeavored to accomplish all that is necessary in a single-stage procedure, whereas others have employed operations of several stages in the hope of reducing the operative risk.

In general, the various plans of surgical procedures can be divided into three main categories: First, a preliminary procedure of some type performed in the hope of reducing the risk associated with subsequent removal of the fistula; second, removal of the fistula without the making of any appreciable effort to prevent further formation of an ulcer or ulcers; third, removal of the fistula in association with performance of partial gastrectomy for the purpose of correcting the immediate condition and also preventing subsequent gastric, duodenal or jejunal ulceration.

Preliminary jejunostomy or colostomy are examples of the first type of procedure. In former years jejunostomy occasionally was employed as a procedure by which it was hoped that the general nutritive state of the patient might be improved prior to performance of the more extensive procedure of removing the fistula. This procedure is only partially successful as a rule, and for several reasons it is not employed now as often as in the past. With the current availability of various vitamin preparations and nutritive supplements for parenteral use, as much usually can be accomplished by the use of such preparations in combination with transfusions of blood and plasma as by the insertion of a jejunostomy tube for feeding purposes. More recently, Pfeiffer and Kent¹⁹ have suggested preliminary colostomy, and in our experience this has been most helpful. Usually, a portion of the transverse colon between the hepatic flexure and the site of the gastrojejunocolic fistula is exteriorized for the purpose of drainage. The improvement which takes place in almost every patient after this procedure is most striking. Generally, there is a definite gain in weight associated with improvement of appetite, amelioration of anemia and lessening of the diarrhea. After performance of colostomy proximal to the fistulous tract, regurgitation of colonic contents

into the stomach and thereby into the small intestine is prevented. Presumably, such regurgitation is at least in part responsible for certain important alterations in the patient's general condition. It appears obvious that fecal material which is constantly retained in the stomach would cause a certain amount of inflammatory reaction in that organ. In addition, much of this fecal material might well leave the stomach through the duodenum and thereby be absorbed to some degree in the small intestine, an abnormal state of affairs which might readily result in deleterious effects. Furthermore, preliminary colostomy has an additional advantage of distinct value in that it eliminates all fecal material from the region of the fistula and permits thorough cleansing of the stomach, jejunum and colon in the vicinity of the fistula prior to performance of the corrective type of surgical procedure. In addition, after closure of the fistula in the colon no fecal material remains in this portion of the bowel, a fact which should improve the chance for good healing. It appears that this factor in itself adds greatly to the safety of removal of the fistula.

Operations directed mainly toward removal of the fistula without performance of an associated procedure of significance to prevent further ulceration are not employed as frequently today as they were formerly. We refer to surgical disestablishment of the gastro-enteric anastomosis, with excision of the fistula and closure of the openings in the stomach, jejunum and colon, associated or unassociated with some type of local operation on the pylorus and duodenum. Although procedures of this type do correct the immediate situation, they offer little protection against the possibility of recurrent ulceration. Usually, procedures of this type have been employed for the patient who is in exceedingly poor condition and for whom it seems advisable to keep the surgical procedure to an absolute minimum. In the past jejunostomy often has been performed in association with this form of operation. With current methods of preoperative preparation, however, jejunostomy does not often seem necessary.

The corrective operation of choice, if the condition of the patient permits it (and generally it will, if proper preliminary attention, both medical and surgical, has been carried out), consists of surgical disconnection of the gastro-enteric anastomosis, excision of the fistula, closure of the openings in the jejunum and colon, and generous resection of the stomach, preferably with the establishment of a posterior Pólya type of gastrojejunal anastomosis. The stomach is joined to the jejunum distal to the site in the jejunum at which the previous gastro-enteric stoma existed. This form of surgical treatment not only eliminates the fistula but also offers definite protection against recurrent ulceration. As a rule, such a procedure can be accomplished without undue risk, provided, as said before, adequate preliminary preparation has been carried out. In our opinion, therefore, the treatment of choice for gastrojejunocolic fistula consists in proper preliminary preparation with the administration of fluids, vitamins and the transfusion of blood if necessary, followed by performance of colostomy proximal to the fistula. After a

period of from three to four months, if the patient is in poor general condition, the fistula is then excised and the stomach is resected. Subsequently, when the patient's condition permits it, the colonic stoma is closed. Employment of a regimen of this type will be followed, we think, by more and more satisfactory results.

Results.—Results of the surgical treatment of gastrojejunocolic fistula in the past have not been satisfactory; however, it seems reasonable to believe that currently more favorable results are being obtained. If the one patient in whom a recurrent gastrojejunocolic fistula formed is considered as representative of two cases in which operation was performed for this condition, it results that there were 11 postoperative deaths in a group of 41 cases (Table IV). This means that the mortality rate was

TABLE IV
RESULTS OF SURGICAL TREATMENT: 41 CASES OF GASTROJEJUNOCOLIC FISTULAE
AMONG 40 PATIENTS

Result	Gastric Resection		Total, 41 Cases
	Performed, 17 Cases	Not Performed, 24 Cases	
Operative deaths.....	2	9	11
No further record.....	10	3	13
Recurrent distress from ulcer.....	1	9	10
Good health.....	3	3	6
Died, unrelated causes.....	1	0	1
Died, massive hematemesis*.....	0	1	1
Total.....	17	25	42

*This patient is also listed as having had recurrent ulcer distress; hence the totals of 25 and 42, respectively in the final two columns.

approximately 27 per cent. There are several factors which seem most important in the reduction of the operative mortality rate. These include a full appreciation of the nutritional deficiencies which this lesion may cause and adequate preoperative preparation to compensate for these abnormalities. In addition, the performance of colostomy, carried out proximal to the fistula, as a preliminary procedure prior to removal of the fistula and gastric resection, reduces the risk of the latter procedure. Postmortem examination, which was performed on ten of the 11 patients who succumbed after operation, revealed that peritonitis and bronchopneumonia were the two complications which contributed most frequently to the fatal outcome.

Of the 30 patients who survived operation, 13 were not heard from after their original dismissal, and consequently the condition of their health is unknown. Of the remaining 17 patients, six were reported to be in good health and ten had had further distress of the ulcerous type, to the time of this report. In this regard it is of interest to consider the result obtained in relation to the type of operation performed. In the entire 41 cases,* gastric resection was performed seventeen times and in the remaining 24

* Counting, as said previously, the one patient who twice underwent operation for gastrojejunocolic fistula as representative of two cases. There were, of course, 40 patients in the series.

cases an operation which did not include gastric resection was carried out. Of the ten patients who experienced further distress of the ulcerous type after operation, only one had undergone gastric resection. In contrast, three of the six patients who were reported to be "cured" had undergone gastric resection. These results substantiate the merit of gastric resection in the presence of gastrojejunocolic fistula.

SUMMARY

Gastrojejunocolic fistula results in a unique mechanical gastro-intestinal shunt. By its mechanism a decrease occurs in the available absorptive intestinal surface. The presence of such a pathologic anatomic pattern is conducive to the development of nutritional disturbances.

In the present series, with two exceptions, gastrojejunocolic fistula in all cases followed gastrojejunal ulcer, the ulcer having been a sequela to a previous operation, usually gastro-enterostomy. In 42 per cent of the 40 cases the fistula occurred within a year after the original operation. In one patient a gastrojejunocolic fistula developed for the second time. All patients were males. The average age of the patient at the clinical onset of the condition was 45 years. The estimated incidence of gastrojejunocolic fistula in the presence of gastrojejunal ulcer varies between 11 and 14 per cent.

Diarrhea and fecal belching or vomiting are the most common symptoms of this condition. Evidence of malnutrition is manifold. Extreme loss of weight and strength and the presence of dehydration, emaciation, hypoproteinemia, nutritional edema, anemia and multiple vitamin deficiency states are characteristic. Such vitamin deficiencies as night blindness, peripheral neuritis, paresthesias, pellagra, glossitis, conjunctivitis, cheilosis, ecchymoses with decreased values for ascorbic acid in the blood and hypoprothrombinemia have been observed. The primary object of preoperative care should be to replenish each of the depleted body nutritional stores, and in so doing, to restore the patient to satisfactory chemical and physical health, so that surgical operation can be performed with the least possible risk.

The surgical treatment of choice for gastrojejunocolic fistula consists of resection of the stomach after the stomach, jejunum and colon have been detached from their fistulous connection. In certain cases preliminary colostomy may be advisable. In the present series of 41 cases (40 patients, of whom one underwent operation twice for fistula) the operative mortality rate was approximately 27 per cent. There are reasons for the belief that this mortality rate will be materially reduced in the future. Results after gastric resection are definitely superior to those which follow mere removal of the fistulous tract in a procedure unassociated with partial gastrectomy.

REFERENCES

- ¹ Gray, H. K., and Sharpe, W. S.: Preoperative Management of Gastrojejunocolic Fistula. *Arch. Surg.*, 43, 850-857, November, 1941.
- ² Thomas, J. R.: Gastrocolic and Gastrojejunocolic Fistulae: Report of Five Cases. *Mil. Surgeon*, 87, 232-243, September, 1940.

- ³ Haller: Quoted by Walters and Clagett.¹²
- ⁴ Zweig: Quoted by Walters and Clagett.¹²
- ⁵ Wolfler: Quoted by Thomas.²
- ⁶ von Hacker; Quoted by Thomas.²
- ⁷ Braun: Quoted by Walters and Clagett.¹²
- ⁸ Czerny: Quoted by Walters and Clagett.¹²
- ⁹ Lahey, F. H.: Diagnosis and Management of Gastrojejunal Ulcer and Gastrojejunocolic Fistula. *Surg. Clin. North America*, 20, 767-780, June, 1940.
- ¹⁰ Walton, A. J.: Gastrojejunal Ulceration. *Brit. J. Surg.*, 22, 33-55, July, 1934.
- ¹¹ Allen, A. W.: An Aseptic Technic Applicable to Gastrojejunocolic Fistula. *Surgery*, 1, 338-348, March, 1937.
- ¹² Walters, Waltman, and Clagett, O. T.: Gastrojejunocolic Ulcer and Fistula. *Am. J. Surg.*, 46, 94-102, October, 1939.
- ¹³ Lahey, F. H., and Swinton, N. W.: Gastrojejunal Ulcer and Gastrojejunocolic Fistula. *Surg., Gynec. & Obst.*, 61, 599-612, November, 1935.
- ¹⁴ Rife, C. S.: Gastrojejunocolic Fistula. *Am. J. Surg.*, 40, 73-88, April, 1938.
- ¹⁵ Robertson, H. E., and Hargis, E. H.: Duodenal Ulcer: An Anatomic Study. *Med. Clin. North America*, 8, 1065-1092, January, 1925.
- ¹⁶ Eusterman, G. B., and Balfour, D. C.: *The Stomach and Duodenum*. Philadelphia, W. B. Saunders Company, 1935, 958 pp.
- ¹⁷ Spies, T. D., and Butt, H. R.: Vitamins and Avitaminosis. In Duncan, G. G.: *Diseases of Metabolism*. Philadelphia, W. B. Saunders Company, chap. 8, 1942, pp. 366-502.
- ¹⁸ Committee on Food and Nutrition, National Research Council: Recommended Allowances for the Various Dietary Essentials. *J. Am. Dietet. A.*, 17, 565-567, June-July, 1941.
- ¹⁹ Pfeiffer, D. B., and Kent, E. M.: The Value of Preliminary Colostomy in the Correction of Gastrojejunocolic Fistula. *ANNALS OF SURGERY*, 110, 659-666, October, 1939.

ACUTE ILEUS*

ANALYSIS OF 130 CASES OPERATED UPON AT THE PRESBYTERIAN HOSPITAL,
NEW YORK CITY, FROM 1936 TO 1939, INCLUSIVE: WITH USE OF MILLER-
ABBOTT TUBE IN 1938 AND 1939

BEVERLY CHEW SMITH, M.D., AND FREDERICK T. VAN BEUREN, M.D.
NEW YORK, N. Y.

THIS REPORT completes a 24-year study of acute ileus at the Presbyterian Hospital by the same authors. The entire study has been divided into six four-year periods. The mortality by periods is recorded in Table I:

TABLE I
MORTALITY BY PERIODS

Period	Number of Cases	Late Cases†	Mortality
1916-1919 inclusive.....	60	81%	66.6%
1920-1923 inclusive.....	80	66%	53.7%
1924-1927 inclusive.....	108	61%	44.4%
1928-1931 inclusive.....	72	71%	48.6%
1932-1935 inclusive.....	130	60%	28.4%
1935-1939 inclusive.....	130	68%	23.8%

Toward the end of this period the following observations were outstanding:

1. The Staff has become, so to speak, more conscious of the possibility of intestinal obstruction in cases of obscure abdominal complaint.
2. The status of enterostomy has been reviewed, indications for the operation clarified, and its employment decreased.
3. Dehydration has been recognized, methods developed to determine the degree present, and various properly prepared solutions have been made easily available for its early correction.
4. Electrolyte deficiency has been chemically studied and early replacements made.
5. Roentgenograms have become a dependable diagnostic modality.
6. Gastric suction has effectively supplemented or replaced lavage, bringing with it chemical electrolytic problems requiring laboratory solution.
7. Intestinal intubation with the Miller-Abbott tube has largely supplemented or replaced gastric suction.
8. Sulfonamide drugs in the peritoneal cavity, parenterally and *per os*, have become accepted therapy.
9. The parenteral peristaltic drugs combined with rectal treatments have been more frequently used.
10. Spinal anesthesia has become, both as to drug and technic, safer and more effective.

* Read before the New York Surgical Society, February 24, 1943.

† Signs and symptoms of obstruction present on admission for 48 hours or more.

11. The percentage of late cases admitted to the Hospital has remained about the same during 24 years, namely, 60 to 69 per cent.

We still believe it advisable that more than one observer engage in such a review. Controversial points of diagnosis were freely discussed before recording.

This 1935-1940 series contains 130 cases which, by chance, is exactly the same as the 1932-1935 group.

This report is not to be confused with that of Leigh, Nelson and Swenson² from the same institution in 1940, concerning the use of the Miller-Abbott tube as an adjunct to surgery of small intestinal obstructions. In their series many cases were diagnosed but recovered with conservative therapy without operation. Their classification was: I. Noninflammatory, (A) paralytic and (B) mechanical obstruction; II. obstruction with peritonitis; and III, obstruction with gangrene, whereas we have continued our original classification of complete, incomplete obstruction, and paralytic ileus. All cases in our series were operated upon. This classification, because of the Miller-Abbott tube, will require subsequent modification in order to include nonoperative cases, which have been diagnosed roentgenologically.

For comparison, a table of the present and previous series is presented (Table II):

TABLE II
COMPARISON OF PRESENT AND PREVIOUS SERIES¹
(1932-1935, Inclusive)

	Total Number	Late Cases	Recovered	Died	Mortality
Series.....	130	60%	94	36	27.6%
Complete obstruction.....	91	63%	78	13	14.3%
Incomplete obstruction.....	26	88%	15	11	42.3%
Paralytic ileus.....	13	69%	1	12	92.3%

(1936-1939, Inclusive)

	Total Number	Late Cases	Recovered	Died	Mortality
Series.....	130	68%	99	31	23.8%
Complete obstruction.....	103	63%	84	19	18.4%
Incomplete obstruction.....	16	88%	14	2	12.5%
Paralytic ileus.....	11	90%	1	10	90.9%

A comparison of these series shows eight per cent more late cases in 1936-1939 group. This should be accompanied, on past experiences, with a higher group mortality, but this is not so. The group mortality was 3.8 per cent less. The predominating factors in these results were the use of the Miller-Abbott tube, continuous gastric suction, and a greater correction of dehydration. Sulfonamide drugs were not used in the last series. The greatest difference in group mortality lies in the incomplete cases, where there was a decrease from 42.3 to 12.5 per cent. This we believe due primarily to the use of the Miller-Abbott tube. The incomplete group reduction was the greatest factor in reducing this series mortality.

ACUTE ILEUS

TABLE III
ANALYSIS OF CASES GROUPED AS TO ETIOLOGY
I. ACUTE COMPLETE MECHANICAL OBSTRUCTION
(Series 1935—1939, Inclusive)

	Number of Cases	Recovered	Died	Mortality
Old postoperative adhesions or bands (2 with gangrene)	47	41	6	12.7%
Recent adhesions or bands (recent peritonitis).....	14	12	2	14.3%
Carcinoma of small intestine and colon.....	8	5	3	37.5%
Strangulated hernia (8 with gangrene).....	28	20	8	28.0%
Volvulus of intestine.....	5	5	0	0
Intussusception.....	1	1	0	0
Totals.....	103	84	19	18.4%

The mortality of this group in the 1932-1935 series was 14.3 per cent, due to a mortality in the old adhesions group of 2.5 per cent in 41 cases. This illustrates that the cases of one series may, by chance, be more desperate than in another comparable one.

TABLE IV
ACUTE INCOMPLETE MECHANICAL OBSTRUCTION
(Series 1935—1939, Inclusive)

	Number of Cases	Recovered	Died	Mortality
Old postoperative adhesions.....	11	9	2	10%
Recent adhesions (recent peritonitis).....	4	4	0	0%
Neoplasm of intestine.....	1	0	1	100
Strangulated hernia.....	1	1	0	0 %
Totals.....	16	13	2	12.5—

In the previous series this group contained 26 cases, with a mortality of 42.3 per cent. The reduced mortality in this group was the result of fewer colon carcinoma cases and the use of the Miller-Abbott tube.

TABLE V
PARALYTIC ILEUS
(Series 1935—1939, Inclusive)

	Number of Cases	Recovered	Died	Mortality
Appendicitis, with acute diffuse peritonitis.....	4	1	3	75%
Mesenteric thrombosis, with peritonitis.....	3		3	100%
Acute diffuse peritonitis (cause undetermined).....	3		3	100%
Acute diffuse peritonitis following pelvic operation....	1		1	100%
Totals.....	11	1	10	90.9%

We define paralytic ileus as those cases with a generalized intestinal distention, without mechanical obstruction, with diffuse peritonitis or other profound pathology, and believe they should not be operated upon except to remove a focus.

The paralytic ileus group mortality of 90.9 per cent indicates its gravity prior to the use of sulfonamide drugs. The mortality in 13 paralytic ileus cases in the previous series was 92.3 per cent. Thus, in eight years, combining these two series, the mortality in 24 cases of paralytic ileus is 91.6 per cent.

TABLE VI
ANESTHESIA
(Series 1935—1939, Inclusive)

	Number of Cases	Recovered	Died	Mortality
Local.....	14	11	3	21.4%
General.....	67	52	15	23.8%
Spinal.....	49	39	10	21.2%
Total.....	130			

Anesthetics should be thoughtfully adapted to each case. Local was employed for the sickest, and the least surgery. Spinal—a single or continuous injection—became the anesthetic of choice. It collapsed intestine, which gave better exposure, ease of closure, and shortened operative time. Disadvantages were lowered blood pressure, anoxemia, and shock, which were combated by ephedrine, intravenous fluids and oxygen.

In complete obstructions fluid replacement averaged 2,900 cc. daily during their acute illness, which was 700 cc. more than the previous series. Daily intake rose for short periods to 5,000 cc. or more, depending upon other pathology.

In the same group, peristaltic drugs were administered in 59 cases, with a mortality of 13.5 per cent. In the previous series they were used in 60 cases, with a mortality of 15 per cent. In the 39 cases they were not used, the mortality was 18 per cent. The Miller-Abbott tube, with rectal treatments postoperatively, decreased their use. In the *early* cases in which gastric and Miller-Abbott tubes were not used they were more effective.

Diagnostic roentgenograms taken with patients sitting up, lying on right and left sides, were positive for gas and fluid levels in 94 per cent of 83 cases operated upon, and inconclusive or negative in six per cent. Those with negative roentgenologic diagnosis, with obstruction, were such early cases that fluid levels were not present, and distension alone was not sufficient to warrant a positive diagnosis. A negative roentgenogram should not delay operation if the history and physical findings are definitive.

The negative roentgenograms were on incomplete obstructions which were not severely distended. None of these died. This would suggest that a negative roentgenogram may indicate a good prognosis. In the presence of a negative film, and clinical evidence of obstruction, exposures should be frequently repeated if the patient is not operated upon.

TABLE VII
ENTEROSTOMY FOR COMPLETE OBSTRUCTION

	Primary	Mortality	Secondary	Mortality
1932—1935, incl.....	30	23.3%	12	23%
1936—1939, incl.....	25	16%	5	60%

The result of combining the last two series of enterostomy cases is tabulated in Table VIII:

TABLE VIII
AGGREGATE STATISTICS OF MORTALITY FOLLOWING ENTEROSTOMY IN THE LAST TWO SERIES
(Series 1932—1935 and 1936—1939, Inclusive)

	No. Cases	Mortality
Enterostomy for complete obstruction.....	72	27.7%
Enterostomy for incomplte obstruction.....	18	59%
Enterostomy for paralytic ileus.....	18	88.8%

Operative Treatment.—In all series, this varied from division of a single band, to colon or small bowel resection for advanced pathology. Enterostomy has been less frequently performed since the advent of the Miller-Abbott tube, particularly in the secondary group, and, recently, less in the primary group. We prefer the Witzel technic, without passing the tube through omentum or suturing intestine to the peritoneum.

The Miller-Abbott tube was first used in The Presbyterian Hospital in December, 1937. Its use has steadily increased, until now, for medical and surgical conditions, it has been employed in approximately 700 cases. We employ a graduate nurse to supervise these tubes and, except for records concerning each case, she has no other duties.

TECHNIC OF EMPLOYMENT OF THE MILLER-ABBOTT TUBE

The tube is used as follows: The nasal passage is inspected for adequate patency; together with the pharynx it is cocainized; the balloon is folded over the tip, well lubricated and passed through the nostril into the stomach. Sipping water aids its more rapid passage. The tip is placed at the pylorus

TABLE IX
SERIES OF 130 CASES—MILLER-ABBOTT TUBE EMPLOYED IN 36, OR 27.6 PER CENT
(Series 1935—1939, Inclusive)

Diagnosis	No. Cases	Died	Mortality
Paralytic ileus.....	5	4	80%
Mechanical complete and incomplete obstruction.....	31	3	9.6%
Totals.....	36	7	19.1%

TABLE X
COMPLETE AND INCOMPLETE OBSTRUCTION
(Series 1935—1939, Inclusive)

	No. Cases	Died	Mortality
Miller-Abbott tube.....	31	3	9.6%
Gastric suction.....	40	10	25%
No tube or suction.....	48	8	16.6%
Totals.....	119	21	17.6%

TABLE XI
PARALYTIC ILEUS

	No. Cases*	Died	Mortality
Miller-Abbott tube.....	5	4	80%
Gastric suction.....	6	6	100%
Totals.....	11	10	90.9%
* Sulfonamide drugs and Miller-Abbott tube.....	1	0	0

TABLE XII
TOTAL SERIES
INCLUDING MECHANICAL COMPLETE, INCOMPLETE AND PARALYTIC CASES
(Series, 1935—1939, Inclusive)

	No. Cases	Died	Mortality
Miller-Abbott tube.....	36	7	19.1%
Gastric suction.....	46	16	34.7%
Without Miller-Abbott tube or gastric suction.....	48	8	16.6%
Totals.....	130	31	23.8%

under the fluoroscope with the tube lying along the greater curvature. It is held lightly by adhesive against the nose (not cheek) for if the slack lay along the greater curvature there is sufficient tubing in the stomach to allow the tip to reach the third portion of the duodenum without introducing more, which may coil or kink.

The following observations concerning the Miller-Abbott tube warrant emphasis:

The progress of the tube can be noted by fluoroscopy and recorded by roentgenograms. Sufficient roentgenray can be administered under such circumstances to affect the skin. Roentgenologic Department observations of the tube should be timed on the chart.

Its rapid passage through the pylorus is facilitated by manipulation under the fluoroscope. This requires experienced observations in a minimum of time. Suction deflates the stomach. Fluids are allowed in order to propel the tube to the pylorus. The patient preferably, but not necessarily, lies on his right side. Once through the pylorus the balloon is inflated with 20cc. of air and allowed to progress of its own accord. Peristalsis carries the inflated balloon downward, causing a noticeable tug. In paralytic ileus the tube may not advance so rapidly, and requires more attention to deflate atonic coils of intestine. In the absence of peristalsis it may be advanced by doctor or patient, but not faster than six inches every two hours, in order to prevent coiling in the stomach. It is frequently irrigated with 40–60 cc. of saline to insure its patency, dilute intestinal contents and deflate successive loops. Patients are so grateful for the relief after gastric deflation that they often cooperate with subsequent tube care. The position of the tube tip can be determined by (1) aspiration of bile or jejunal content; (2) the time required for fluid by mouth to be aspirated; and (3) by lack of resistance to inflation of the balloon if it remains in the stomach. We do not hesitate to transport sick cases to fluoroscopy for manipulation of the tube if it has not passed out of the stomach in 6–12 hours. During this time continuous gastric suction is emptying the stomach.

The time, amount and character of the aspirated fluid should be charted, together with hematocrit, plasma specific gravity, plasma protein and blood chloride determinations. Chloride replacement should be approximately five grams for each liter aspirated. Continuous aspiration with the tube tip in the jejunum returns one-half to two-thirds of the fluid taken by mouth,

whereas about one-third returns with the tip in the ileum. Frequent fluoroscopic or roentgenologic examinations determine the site and rate of progress of the tube.

Often, regurgitated loop-content requires withdrawal of the tube tip into that loop, aspirating it, and again allowing the tube to advance. The stomach may become distended while the tube tip is deflating the jejunum, in which case a gastric lavage by a Levin tube may be necessary. The tube should be left *in situ* until (1) the obstruction is relieved or passed; (2) it has reached the cecum; or (3) the character of the aspirated fluid becomes normal intestinal contents, and the Roentgenologic Department agrees that its diagnostic possibilities have been exhausted.

The tube was left *in situ* for an average of five and one-half days. The longest time was 39 days. The average fluid recovered was 3,300 cc. for the ordinary case. The largest amount was 36,000 cc. in 27 days.

At operation, it has served as a guide to the site of obstruction.

Successful intubation deflates, improves blood supply and neuromuscular mechanism of peristalsis, permits absorption and correction of fluid and electrolyte imbalance, diagnosis of site and extent of local pathology, and converts a toxic, distended late case into either a comparative early or a nontoxic, nonobstructed one.

With the tube *in situ*, high protein fluids can be given and hypoproteinemia be corrected by other than plasma and whole blood. A tube which has coiled into a knot may remain patent but may not pass a partial obstruction. During intubation, clinical signs and symptoms of compromised blood supply of intestine must be constantly kept in mind and watched for. They are often difficult to ascertain and may occur in the absence of fever, leukocytosis and tenderness. The development of gangrene of the intestine while an ileus toxemia is being combatted, constitutes the greatest danger associated with the Miller-Abbott tube. Fortunately, if patients are closely watched, this occurs infrequently.

The tube may be retarded by a kink, band, foreign body, tumor, inflammation of the wall or extrinsic pressure. Following deflation, barium may be injected through the tube and films may reveal the nature of the local pathology. The fact that the barium advances but the tube does not, confirms the degree of the mechanical obstruction. Multiple obstructions may be demonstrated. A site of cryptic bleeding may be localized by gross appearance or chemical tests upon aspirated fluid.

The following adverse incidents have occurred in our experiences with this tube:

Patients may not tolerate it. Irrational patients may remove it, and restraint increases their restlessness. It is difficult, almost impossible, to get a Miller-Abbott tube to pass through a gastrojejunal stoma. It may be coughed or vomited up. It is poorly tolerated in the presence of pneumonia. Nasal pathology makes it locally uncomfortable. The nasopharyngeal portion

should be cleansed of dried secretions, oiled and replaced several times a day. Esophagitis has been reported, but it has not manifested itself clinically in our cases. Laryngitis has not been a serious complication. The tube may not pass through the pylorus because of gastric atony, distension or local pathology. It has been regurgitated from the duodenum. Inflation of the balloon prevents this. It has coiled and knotted in the stomach and intestine. The balloon has been broken by overinflation and the injection of fluid. The orifices for fluid and air should be plainly marked. The tip may become lodged in a partial obstruction and convert it into a complete one. An inflated balloon may act similarly. The small intestine has intussuscepted itself on the tube. It has delayed operation and permitted gangrene of the intestine to occur during the period of treatment. Incorrect interpretation of the patient's response to treatment, and delay in making these observations, may unnecessarily delay operation. Large bowel treatments (lavage, *etc.*) administered when the tube is in the terminal ileum or cecum have been recovered through the oral end of the tube. Fluids given for nourishment, particularly those containing milk, may block the tube and necessitate its withdrawal for cleansing.

Confronted with an early case of obvious intestinal obstruction, without severe distension, confirmed roentgenologically, and without clinically evident dehydration, one must decide whether emergency operation or Miller-Abbott tube intubation should be undertaken on the merits of the particular case. Given a late case, similarly proven, distended, and dehydrated, the Miller-Abbott tube should seriously be considered for preoperative treatment, for its greatest usefulness has been observed in this group. If signs and symptoms of intestinal gangrene are suspected or are evident, operative delay because of Miller-Abbott tube treatments will produce a fatality.

For resections of obstructed as well as unobstructed right colon carcinoma cases, this tube has largely replaced enterostomy as a decompressing procedure and has permitted more successful one-stage operations.

DISCUSSION

This last group (1935-1939) of a 24-year series showed the lowest mortality, we believe, due to an earlier diagnosis, aided largely by roentgenology, adequate fluid and electrolyte replacement, better anesthesia, the use of peristaltic drugs and rectal treatments, and, particularly, the employment of the Miller-Abbott tube.

The Miller-Abbott tube and gastric suction were not employed in early cases with simple pathology who had an easy, short operation, whose intestine showed peristalsis, and who responded to drugs and rectal treatments.

Small intestinal roentgenologic studies should be made upon cases of obstruction which have recovered without operation. Findings may indicate an interval exploration.

Early diagnosis of obstruction remains difficult. Roentgenologic examina-

tion has been the single, outstanding, dependable diagnostic aid. Diagnosis should be made before the roentgenologic findings become positive, but this is often difficult. Obstruction occurring during another illness is even more difficult to diagnose.

The same type of errors of diagnosis and treatment seem to recur in each series, but are least outstanding in the latest series.

Delay in certain instances is unwarranted in attempting to make a new treatment work. We have seen this, in turn, with hypertonic saline, peristaltic drugs and the Miller-Abbott tube.

Prolonged operations upon seriously ill, dehydrated, distended patients is just as dangerous today as it was a quarter of a century ago.

Injudicious choice of anesthesia may be fatal. It should be adapted to the patient.

A scar of a previous abdominal operation remains an indication of a possible obstruction in an abdominal complaint.

We are still impressed by the number of obstructions that follow abdominal gynecologic operations.

The positive roentgenogram may not follow the suspected clinical signs of obstruction for some time, but it may be positive earlier than the clinical diagnosis. When the roentgenologic diagnosis is not positive, the entire situation should be reviewed by a senior observer.

As important as electrolytic balance is, it can be further upset by overtreatment.

Witzel enterostomy technic has demonstrated the following as compared to that of Kader:

- (a) Fewer have had to be closed operatively.
- (b) They have functioned better and less has escaped around the tube.
- (c) With removal of the tube the intestinal opening has leaked less and closed more quickly.

Enterostomy as an adjunct to the treatment of intestinal obstruction should not be discarded. It has been more effective as a primary than secondary procedure.

Principles concerning viable and nonviable intestine should be reviewed before closing an abdomen.

Chart records could be more easily classified if there was, in the written operative procedure, a concise note as to the duration of preoperative symptoms, the presence of collapsed and distended intestine, an exact description of the condition of the intestine, and the obstructing mechanism. The last, at times may be most difficult.

Aerobic and anaerobic cultures should be taken of peritoneal fluids and resection sites at the completion of the operation.

Six to eight grams of sulfanilamide should be left in the abdomen in cases with an odoriferous fluid or in which the intestine has been opened. It is not a good substitute for poor surgery.

Too many instances of secondary peritonitis have followed contamination from hernia sacs. Better protection should be practiced.

Richter herniae are dangerous because of difficulty of diagnosis; even the roentgenogram misses them, and the segment of intestine involved is often nonviable.

Methods of preventing peritoneal adhesions, including the size and position of the incision through the abdominal wall, are still an important part of the ritual of any abdominal operation.

REFERENCES

- ¹ van Beuren, F. T., Jr., and Smith, Beverly.: Acute Ileus. *ANNALS OF SURGERY*, 107, 321, 1938.
- ² Leigh, O. C., Jr., Nelson, John H., and Swenson, Paul C.: The Miller-Abbott Tube as an Adjunct to Surgery of Small Intestinal Obstructions. *ANNALS OF SURGERY*, 111, 186, 1940.

ISLET CELL CARCINOMA OF PANCREAS, WITH METASTASIS

HAROLD A. HANNO, M.D., AND ROLAND W. BANKS, M.D.

PHILADELPHIA, PA.

FROM THE DEPARTMENTS OF PATHOLOGY, GASTRO-ENTEROLOGY, AND SURGERY, GRADUATE HOSPITAL,
UNIVERSITY OF PENNSYLVANIA, PHILADELPHIA, PA.

A NUMBER of islet cell tumors of the pancreas, both benign and malignant, have been recorded in the literature. Nicholls,⁴⁵ in 1902, reported the first unequivocal islet tumor, an adenoma discovered as an incidental finding at autopsy. Fabozzi,¹⁸ in 1903, described five cases, four of which showed involvement of other organs. During the next few years additional cases of islet cell adenoma were found.^{20, 28, 44, 12} Vecchio,⁵³ in 1914, described an islet cell tumor found in aberrant pancreatic tissue. Lang³⁰ was the first to report the finding of multiple adenomata of the pancreas. Reviewing the subject in 1926, Warren⁵⁴ could find only 16 reports of islet cell tumors, none of which involved distant or neighboring organs, and he added four cases of his own. In none of the cases which he reported was a clinical summary included. He ventured the opinion that these lesions "probably never give rise to trouble during life and have no clinical significance."

However, following the discovery of insulin by Banting and Best,² in 1922, and the recognition of the effects of insulin overdosage,^{22, 3} the tumors of the islet cells of the pancreas soon were resurrected from the limbo of mere pathologic curiosities. Interest in these tumors mounted because of the clinical picture which some of them were found to present.

Credit belongs to Harris²⁶ for suggesting, in 1924, the possibility of hypersecretion of insulin as the causative factor in certain cases of spontaneous hypoglycemia. This hypothesis was confirmed when, in 1927, Wilder, Allan, Power, and Robertson⁶¹ reported their case of the physician who clinically presented a typical picture of severe hypoglycemia and who showed at operation and at autopsy an islet cell tumor of the tail of the pancreas, with metastases to the liver and the regional lymph nodes. Assay of the tumor tissue revealed the presence of a markedly increased insulin content. Warren⁵⁵ regarded the demonstration of insulin in the tumor metastases in this case as laying the foundation for the clinical entity of hyperinsulinism and he considered it as the final proof of the etiologic relationship of insulin lack to diabetes mellitus. Since the report of Wilder and his associates, the presence of insulin in increased amounts in the tumor tissue in cases of islet cell neoplasm, with hypoglycemia, has been demonstrated several times.^{14, 7, 30}

The incidence of tumors of the islands of Langerhans is a matter of some question. Whipple and Frantz,⁵⁹ in 1935, reported only 61 cases, only one of which showed metastases. Three years later Whipple⁵⁷ listed 74 cases of islet cell tumor, with hypoglycemia, and, in 1940, Frantz²¹

was able to gather 96 cases. In 1941, Keating and Wilder³⁷ reported 106 cases. This number has been increased to 134 in Whipple's⁵⁸ recent article. More recently a number of additional cases have been recorded.^{38, 47, 48, 42, 63} Autopsy estimates as to the frequency of islet cell tumors vary from one per 10,000¹⁰ to five in 4,010 consecutive necropsies.⁴⁶ It is of interest to note, in passing, that an islet cell adenoma has been found in a mouse³¹ and that malignant neoplasms, with metastases, have been described in dogs on two occasions.^{50, 8}

Islet cell adenomata are of interest because of the clinical hypoglycemia which often occurs. Campbell, Graham and Robinson¹⁰ state that in only 20 per cent of the cases of islet cell tumor does hypoglycemia exist. In the series of Whipple and Frantz,⁵⁹ however, 31 tumors unassociated with clinical hypoglycemia were found at autopsy as opposed to 30 such tumors accompanied by hypoglycemia; and in Duff's¹⁶ group of 90 case reports there were 64 hypoglycemic cases. The absence of thorough clinical records may well account for at least a portion of the number of cases of islet cell tumor reported with no mention of hypoglycemia.

Undeniable islet cell carcinoma with involvement of neighboring structures or metastases to distant organs is rare. A number of cases of islet cell tumors involving only the pancreas have been thought to be malignant on histologic examination.^{30, 19, 52, 43, 13, 35, 4, 53} Frantz²¹ lists 21 cases in her total of 91 islet cell neoplasms limited to the pancreas. These tumors have been variously labeled malignant, questionably malignant, adenocarcinoma Grade 1, and of low grade malignancy, because, microscopically, they showed a number of the characteristics associated commonly with malignancy. Lack of capsulation, incomplete encapsulation, blood vessel invasion, and cellular anaplasia with frequent mitotic figures have been described in these tumors. However, the 15 patients in Frantz's group of tumors of questionable or low-grade malignancy who survived surgery have shown no metastases or recurrences in follow-ups of from eight weeks to ten years, only four cases having follow-ups of less than a year. According to Duff,¹⁶ the patient of Howland, Campbell, Maltby, and Robinson,³⁰ who was operated upon in 1929 for a "malignant" islet cell tumor limited to the pancreas, was reported well 12 years following surgery and 19 years after the onset of his symptoms of hypoglycemia. Frantz²¹ expressed doubt as to whether all of the tumors in this "locally malignant" group constitute real malignancies, although she admitted that metastases might occur at later dates. Duff,¹⁶ and Brunschwig⁹ concur in the belief that a histologic appearance of malignancy in cases of islet cell tumor is not a valid index of malignancy. This point deserves emphasis. The present authors feel that, as far as can be determined at present, the only true criterion of malignancy in islet cell neoplasms is the presence of involvement of other organs by direct extension or by metastasis, the microscopic characteristics of the tumor tissue notwithstanding. Further reports of longer follow-ups in questionable cases are, of course, to be desired.

A careful search of the literature to date (December, 1942) has revealed only 21 cases of islet cell tumor with involvement of other organs, to which group we should like to report another. These cases, with the available pertinent data, are tabulated in Table I. Willis'⁶² unusual case of widespread malignancy may possibly represent an instance of islet cell carcinoma. We are omitting the case reported by Berardinelli⁶ because this is, in all probability, a malignancy of the common acinar type. Balinger's¹ report of a widespread malignancy in which the pancreas was not involved is not included in the tabulation because his surmise that the primary tumor arose from ectopic pancreatic tissue in the liver may not be valid.

It is of interest to note that Fabozzi,¹⁸ in describing his five cases of islet cell tumor, apparently did not realize that he was dealing with an unusual type of neoplasm, for the conclusion which he drew from his observations was that malignant tumors of the pancreas nearly always arise from the cells of the islands of Langerhans.

Case Report.—B. G., white, male, age 68, was admitted, September 10, 1942, to the Graduate Hospital on the Gastro-Intestinal Service of Dr. H. L. Bockus. His chief complaint was upper abdominal pain. He dated the onset of his illness to 21 months ago, at which time he struck himself with a wrench and broke several ribs. After two weeks in bed he had no complaints until 19 months before admission when he experienced a severe, sharp pain in the left lower chest. This was accompanied by dyspnea, fever, and chills, but there was no cough or hemoptysis. A diagnosis of pleurisy was made. It was at this time that he first noted frequent cold sweats accompanied by marked weakness which would come on at about 6 A.M. Though never unconscious, on one occasion he could not speak. His wife would give him milk and bread and he would feel much better. Because of his pleurisy he was treated by bed rest for nine months, during which period he had marked swelling of both legs.

The upper abdominal pain began about nine months prior to admission. It was dull and aching in character, not very well localized, and involved first the right side and then both sides of the upper abdomen, but for the most part was epigastric in location. Though the pain was worse when he was hungry, food or soda gave no noticeable relief, but belching seemed to alleviate the discomfort. The pain was aggravated by deep inspiration. He had lost about 30 pounds in weight during the year prior to hospitalization, and associated with this was loss of strength and energy. He complained of exertional dyspnea, but gave no history of vomiting, jaundice, clay-colored or tarry stools, or a change in bowel habit. Since their onset nine months previously, the episodes of morning weakness, relieved by food, have recurred frequently.

Physical Examination.—This revealed a rather florid-faced, elderly white male who showed evidence of marked weight loss. He was in no acute distress and the sensorium was clear. The scalp, eyes, ears, and nose were essentially negative. There was partial edentia, and the tongue was rather red and showed very slight atrophy of the markings at the margins. The lungs were moderately emphysematous. The heart size was within normal limits, and the rate, rhythm, and sounds were normal. B. P. 142/80. Examination of the abdomen revealed a large, hard, irregularly rounded, dome-shaped mass in the epigastrium. The mass was tender and moved very slightly with deep respiration. The liver edge was palpable three centimeters below the right costal border, and the area of splenic dullness was enlarged. Rectal examination disclosed a *moderately enlarged prostate, which was thought to be benign*. Bilateral hydrocele was noted, and there was slight pitting edema of the right ankle. Neurologic examination was negative.

TABLE I
A TABULATION OF CASES OF ISLET CELL CARCINOMA, WITH INVOLVEMENT OF OTHER ORGANS

Case No.	Author	Year	Age	Sex	Survival After		Site in Pancreas	Size of Tumor	Involvement of Other Organs
					Onset of	Symptoms			
1.	Fabozzi ¹⁸	1903	65	?		No clinical data	Hypoglycemia	Head	Orange-sized
2.	Fabozzi ¹⁸	1903	30	M.		No clinical data	No clinical data	Head	Not mentioned
3.	Fabozzi ¹⁸	1903	56	M.		No clinical data	No clinical data	Tail	"Head of fetus"
4.	Fabozzi ¹⁸	1903	?	?		No clinical data	No clinical data	Head	Not mentioned
5.	Zanetti ⁶⁵	1927	56	M.		No clinical data	No clinical data	Entire pancreas	Not mentioned
6.	Wilder, <i>et al.</i> ⁶¹	1927	40	M.		21 months	Present	Tail	Not mentioned
7.	Lloyd ⁴⁰	1929	?	?		No clinical data	No clinical data	Not mentioned	Not mentioned
8.	Hamdi ²⁵	1932	52	M.		No clinical data	No clinical data	Tail	2 x 2.5 cm.
9.	Judd, Faust, and Dixon ³⁶	1934	18	F.		4 months	Present	Not mentioned	Not mentioned
10.	Jacobsen ³³	1934	36	M.		1 to 2 years	Present	Head	Grapefruit-sized
11.	Bickel, Mozer, and Juncet ⁷	1935	56	M.		10 mos. (approx.)	Present	Body and tail	7 x 2.5 x 5 cm.
12.	Evangelisti ¹⁷	1935	65	M.		No clinical data	No clinical data	Body and tail	Not mentioned
13.	Cragg, Power, and Lindem ¹⁴	1937	41	F.		7 months	Present	Entire pancreas	Not mentioned
14.	Joachim and Banowitch ³²	1938	31	F.		3 months	Present	Distal half	"Tangerine-orange"
15.	Seckel ^{19*}	1939	36-38	M.		1 year	Present	Proximal half	4 x 2 x 2 cm.
16.	Duff ¹⁵	1939	32	M.		3 months	Absent	Entire pancreas	Not mentioned
17.	Duff ¹⁶	1939	60	M.		7 months	Absent	Entire pancreas	Not mentioned
18.	Duff ¹⁵	1939	45	M.		5½ months	Absent	Entire pancreas	Not mentioned
19.	Flinn, <i>et al.</i> ²⁰	1941	45	F.		6 mos. (approx.)	Present	Head	Not mentioned
20.	Gray ^{24†}	1942	48	F.		4½ years	Present	Tail	1.8 x 1.8 x 1.3 cm.
21.	Quarrier and Bingham ⁴⁷	1942	73	M.		3½ weeks	Present	Tail	3 cm. in diameter
22.	Hanno and Banks	1943	68	M.		19 months	Present	Tail	8 x 8 x 6.5 cm.

*This case has been reported also by Brunschwig,⁹ Gomori²³, and Cannon.¹¹

†This case has been reported also by Joslin *et al.*³⁴

‡Operative findings.

Note: All but two cases were autopsied.

Laboratory Data.—Erythrocytes, 5.1 millions; hematocrit, 39; hemoglobin 13 grams (78%); leukocytes 6700. with 72% neutrophils, 7% monocytes, 1% basophiles, and 20% lymphocytes; urinalysis was negative except for traces of albumin and occasional leukocytes; flocculation and complement fixation tests for syphilis were negative; serum bilirubin was less than 0.2 mg. per cent; prothrombin time by Quick's method 13 seconds (100%); serum phosphatase 5.2 and 4.4 Bodansky units; blood urea nitrogen 17 mg. per cent; cholesterol 216 mg. per cent; fasting blood sugar 54 mg. per cent, serum albumin 3.85 grams per cent; serum globulin 2.79 grams per cent. There was seven per cent dye retention 30 minutes after the intravenous injection of two milligrams of bromsulfalein per kilogram of body weight. The stools were repeatedly negative for occult blood and positive for bile. Gastric analysis revealed 48 units of free acid and 74 units of total acid at the end of one hour. Roentgenologic study of the colon was negative and a barium progress meal disclosed only some displacement of the stomach to the left.

The patient was placed on a smooth meat-free diet and given a maintenance dose of one and one-half grains of digitalis daily. At 1:30 A.M. the third morning after admission, he began to moan and perspire profusely, complaining also of weakness. He was unconscious by the time he was seen by a physician. A blood sugar was taken and 25 cc. of 50 per cent glucose was administered intravenously, whereupon the patient "awoke" quickly, sat up in bed, and drank some orange juice. The blood showed 44 mg. per cent of sugar.

At 5:00 A.M. the following morning a similar episode occurred. Six minims of adrenalin subcutaneously was without effect, but 15 cc. of 50 per cent glucose revived him. The next morning the blood sugar at the time of another attack was 21 mg. per cent. That same day, at 11:00 A.M., he had another period of unconsciousness which was quickly controlled by intravenous glucose.

Because of the repeated attacks of hypoglycemia, he was placed on a high fat, high protein diet with a small midnight feeding. No further episodes of hypoglycemia occurred while he was on this regimen.

After an eight-hour fast a glucose tolerance test was performed, using 100 grams of glucose dissolved in water. The values obtained are shown below. At the beginning of the test the patient complained of weakness and was perspiring. Again at the end of five hours he began to perspire profusely and complained of weakness. The test was not carried out for the full six-hour period because between the fifth and sixth hours the patient became unconscious and had mild generalized convulsions, which promptly responded to intravenous glucose.

Fasting—	34 mg. per cent of sugar
½ hour —	73 mg. per cent of sugar
1 hour —	104 mg. per cent of sugar
2 hours—	151 mg. per cent of sugar
3 hours—	133 mg. per cent of sugar
4 hours—	69 mg. per cent of sugar
5 hours—	32 mg. per cent of sugar
5 to 6 hours—	26 mg. per cent of sugar

Operation.—September 23, 1942: A celiotomy was performed by Dr. Walter Estell Lee. The liver was found to be enlarged and studded with circumscribed whitish-gray masses which varied in size from that of a pea to that of a walnut. A large mass posterior to the peritoneum, and just inferior and adherent to the spleen, was palpated. The exact origin of the mass could not be definitely determined. A biopsy of one of the liver nodules was taken, and the abdomen closed.

Pathologic Examination.—Dr. Eugene A. Case. "The specimen received is a small biopsy of a tumor nodule in the liver. Very little liver tissue is present, its place being taken by an epithelial tumor whose cells have a well-stained, rounded

nucleus with scattered granules of chromatin and a considerable clear cytoplasm. Some of the cells are elongated and some rounded or polyhedral, and they are arranged in nests or processes suggesting glandular origin. Mitosis occurs but is not frequent. The fibrous stroma is rather loose in texture and fairly abundant. From the clinical history it is highly probable that this tumor arose from cells of the islands of Langerhans, though we were unable to demonstrate the granules found in these cells. *Pathologic Diagnosis:* Metastatic carcinoma of islet cell origin."

The patient's postoperative course was rapidly downhill. Glucose intravenously either every four hours as a 50 per cent solution or continuously as a 10 per cent infusion was necessary to prevent severe hypoglycemia. He developed dyspnea and tachycardia and went into shock several times during the second postoperative day, being revived each time by intravenous glucose. That evening he went into shock once more and expired a few moments later. Postmortem examination was performed by one of us (H. A. H.) 16 hours after death.

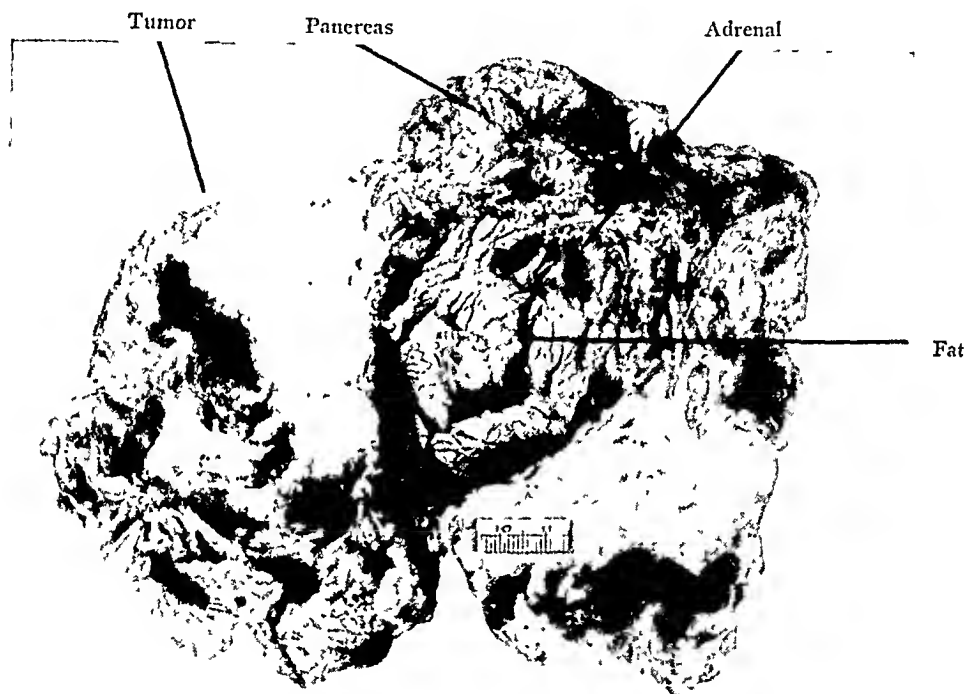


FIG. 1.—The tumor mass and adjacent tissue has been cut in half and folded back. The distal half of the pancreas can be seen to be continuous with the tumor mass proper, and the hemisectioned left adrenal is visible in the fatty tissue between the halves of the tumor.

Necropsy Findings.—Gross: Recent midline abdominal surgical wound; bilateral avascular pleural adhesions; healed calcified tuberculosis of the left lung; pulmonary congestion; coronary sclerosis; atherosclerosis of the aorta; retention cysts of the kidneys; possible benign nephrosclerosis; benign prostatic hyperplasia; bilateral hydroceles; bilateral cysts of the hydatids of Morgagni; carcinoma of the tail of the pancreas; and widespread metastatic carcinoma of the liver.

When the abdomen was opened the stomach was found to be deviated to the left, and in the left upper quadrant was a large firm mass the size of a small grapefruit. The spleen was firmly adherent to the upper and anterior surfaces of the mass and the splenic flexure of the colon was adherent to it anteriorly and inferiorly. The omentum was adherent to the tumor mass anteriorly, and posteriorly the left adrenal was attached to the mass by a thickness of soft fatty tissue. The left kidney was freely movable with respect to the tumor and adherent structures and was not involved by the neoplasm. Posteriorly, the pancreas was found to be directly continuous with

the tumor mass; there was no line of cleavage between the mass proper and the distal portion of the pancreas. The head and the body of the pancreas were grossly normal; the tumor involved the tail.

The tumor mass was roughly rounded, but presented a number of nodular projections. On the whole, it was firm and whitish, but several soft areas were noted which, on section, were found to contain a sticky, purplish material. The cut surface of the tumor revealed areas of focal hemorrhage and presented a fasciculated appearance. The mass (Fig. 1) measured $8 \times 8 \times 6.5$ cm., and the combined weight of the pancreas and tumor was 370 grams.

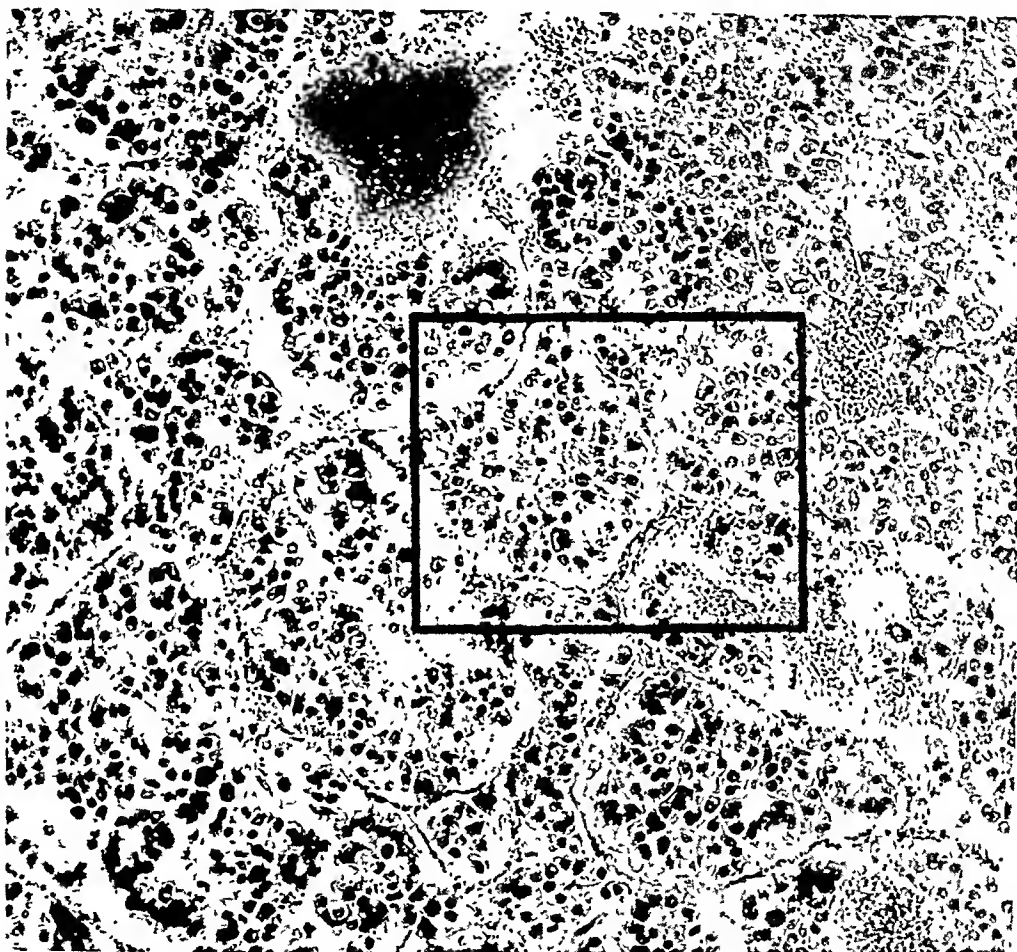


FIG. 2.—A photomicrograph of the tumor tissue in one of the metastatic nodules in the liver. The tendency toward an acinar arrangement is pronounced, although a sheet-like formation of the cells can be seen at the left. The resemblance of the tumor cells to the cells of the islands of Langerhans is striking. Areas of focal hemorrhage are present. ($\times 150$ —Hematoxylin and eosin stain)

The liver was enlarged and weighed 2500 grams. The parenchyma was brownish in color and firm in consistency. The liver was riddled throughout with whitish, circumscribed nodules of varying size, from that of a pea to that of a lime. The largest of these masses was located in the right lobe and measured seven centimeters in diameter. On the section, the larger of the nodules were found to contain a sticky, bluish-red material, which was considered as evidence of degeneration.

Both adrenals were entirely negative on section. The bowel was normal except for the area of the splenic flexure which was adherent to the tumor mass; only the serosa was involved, and the bowel wall was intact. No lymphadenopathy was found.

Microscopic.—The tumor tissue was found to be made up of sheets and nests of small polyhedral cells with pale basophilic cytoplasm. The cells varied somewhat in size and shape, and in some areas columnar cells were common. The nuclei were large and oval or round. The majority were vesicular, but many were pycnotic and hyper-

chromic. The nucleoli were prominent. Large multinucleated cells were occasionally seen. Mitotic figures were very few. In some areas the cells tended toward an acinar arrangement which was sometimes marked; in other places they were arranged in sheets or thin strands. The resemblance of the tumor cells to the cells of the islands of Langerhans was striking. The supporting stroma consisted of ill-defined and pale-staining collagenous material which was found in thin strands or, less frequently, in wide trabeculae. Many small blood vessels were seen, and focal hemorrhage and degeneration were noted.

The pancreas itself was histologically normal. The islet cells were smaller than the cells composing the tumor.

The metastatic nodules in the liver presented the same microscopic characteristics as did the parent tumor tissue (Figs. 2 and 3). The supportive stroma was more abundant in the hepatic lesions.

The microscopic examination of the other organs was essentially negative.

Attempts to demonstrate specific granules in the cells of the tumor tissue were inconclusive. Assay of the tumor tissue for insulin content was not performed.

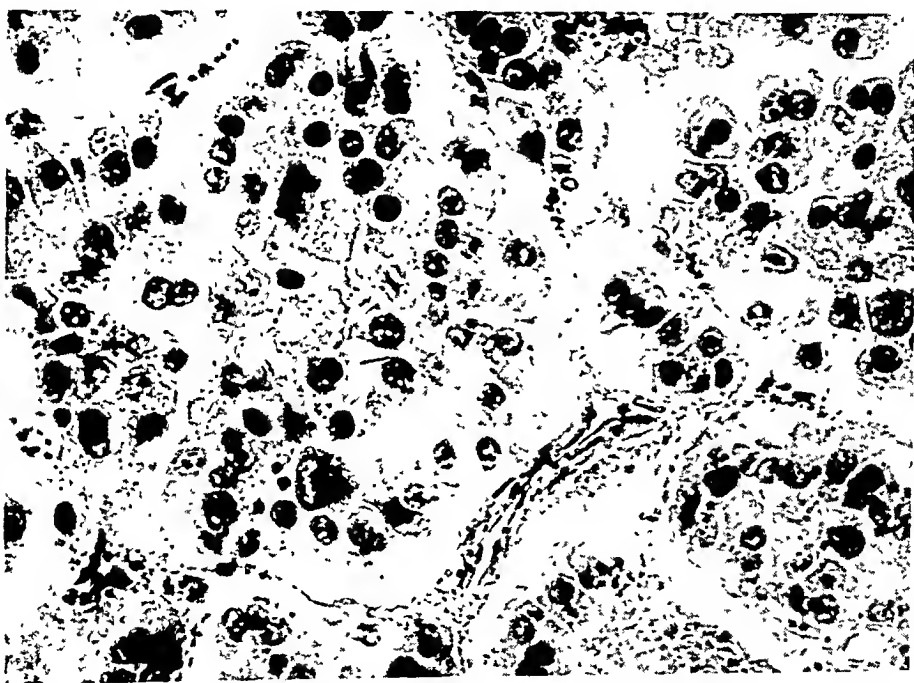


FIG. 3.—A higher-powered view of the blocked-in portion of the field shown in Figure 2. The vesicular and hyperchromatic types of nuclei can be seen, and the nucleoli are prominent. (x 620—Hematoxylin and eosin stain)

DISCUSSION

An analysis of the various features presented in the series of cases of islet cell carcinoma tabulated in Table I is of both pathologic and clinical interest.

Pathologically, the size of the pancreatic masses varied considerably. The smallest tumor measured 1.8 x 1.8 x 1.3 cm.; the largest, with recorded dimensions, measured 8 x 8 x 6.5 cm., although lesions the size of a fetal head and the size of a small grapefruit have been reported.

So far as the site of the tumor in the pancreas is concerned, five of them occurred in the head, six in the tail, two in the head and body, and two in the tail and body. The entire pancreas was involved in five instances. In

no case has the body of the pancreas alone been the site of an islet cell carcinoma. Maximov and Bloom⁴¹ state that the islands of Langerhans are somewhat more numerous in the tail of the pancreas, and Duff¹⁶ has pointed out that islet cell adenomata are found most frequently in the tail. In the series of islet cell malignancies, however, the head and the tail have been the site of the tumor in almost an equal number of instances.

Grossly, the lesions were, as a rule, fairly well circumscribed, although in some cases surrounding adhesions and infiltration of neighboring organs have been described. The tumors were whitish or yellowish in color, and generally firm in consistency. Areas of focal hemorrhage and necrosis have been mentioned. Nodularity of the tumor mass was the rule. The metastatic lesions have presented much the same appearance grossly as did the primary pancreatic tumors.

Microscopically, the appearance has been essentially identical in all cases. The tumor tissue was composed of small polyhedral or columnar cells arranged in places in sheets, clusters, or strands, and characteristically showing a decided tendency toward acinar formation. The resemblance of the tumor cells to the cells of the island of Langerhans has been remarked upon repeatedly. Some degree of variability in the size of the cells has been present. The cytoplasm of the tumor cells has taken either a pale basic or a pale acid stain, more commonly the former. A tendency toward infiltration of the adjacent pancreatic parenchyma and cellular anaplasia of various degrees have been described. The nuclei of the cells have been vesicular or hyperchromatic. Multinucleated cells have been described in two instances (Cases 11 and 22). Mitotic figures have, as a rule, been infrequently found. In four instances staining for specific granules has been successfully accomplished (Cases 14, 15, 10 and 20). The supporting stroma has varied from delicate strands to wide bands of connective tissue. The metastatic lesions have shown, histologically, essentially the same characteristics as the parent tumor.

Metastases were widespread and generalized in five cases. The liver was involved metastatically in 18 cases, and the regional nodes in 11.

In three of the cases reported insulin assay of the tumor tissue has been successful (Cases 6, 11 and 13). With respect to the benign islet cell adenomata, successful insulin assay has been reported in at least eight instances.^{47, 38, 21}

From the clinical point of view a number of interesting facts are to be gained from a survey of the cases of islet cell carcinoma reported:

Of 19 cases in which the sex of the patient could be ascertained, 14 occurred in males and five in females.

The age of the youngest case reported was 18; that of the oldest 73. The average age of the patients was 47.8 years. Six cases occurred in persons 39 or under; ten in the age-group of 40 to 60; and four in patients 61 or over.

Figures of the duration of survival after the onset of symptoms were

available in 14 of the 22 cases. The shortest period of survival was three and one-half weeks; the longest recorded was four and one-half years. Five patients lived a year or more after their symptoms began; and six died in six months or less. The average duration of life once symptoms were noted was 11.9 months.

In all of the 11 cases, where adequate clinical data was available, hypoglycemia of marked degree was present and the progressive increase in the severity and the frequency of the hypoglycemic episodes constituted the principal clinical feature. In the three cases mentioned briefly by Duff,¹⁵ the absence of hypoglycemia was remarked upon. In the hypoglycemic cases blood sugar levels in the low twenties have not been uncommon; in one case a blood level of 16 mg. per cent was noted. According to Womack⁶⁴ "cancer of the islet cell type presents the most profound states of hypoglycemia that are encountered clinically." The clinical and pathologic aspects of hypoglycemia have been thoroughly reviewed by several authors.^{60, 64, 56}

Jaundice has been noted in only two instances (Cases 1 and 2). These cases were among the group of 12 tumors which involved the head, five of which were limited to the head alone. Berk,⁵ in his review of pancreatic carcinoma of the common acinar type, found jaundice in 81.3 per cent of the malignancies involving the head of the pancreas.

In two of the 11 cases, where adequate clinical data was obtained, there was a history of diabetes mellitus prior to the onset of the symptoms of hyperinsulinism (Cases 10 and 11). One of the five cases reported by Harris²⁶ in his original article had had glycosuria, and Herxheimer,²⁹ Heiberg,²⁷ and Smith and Seibel,⁵¹ have reported islet cell adenomata in diabetics. It is of interest to note, in passing, that Berk,⁵ in his review of the acinar variety of pancreatic malignancy, found that 6.9 per cent of the patients in this group had antecedent diabetes, whereas the incidence of diabetes mellitus in the cancer group, at large, he placed at one to two per cent.

SUMMARY

1. The literature on the subject of carcinoma of the islet cells of the pancreas has been reviewed.

2. It has been pointed out that, at present, the only valid criterion of malignancy in cases of islet cell tumor is the presence of metastases or invasion of neighboring organs, the histologic characteristics of the tumor notwithstanding.

3. Twenty-one cases of islet cell carcinoma with involvement of other structures have been culled from the literature and an additional case added. An analysis of these cases has been presented.

We are indebted to Drs. Eugene A. Case, Henry L. Bockus, and Walter Estell Lee for permission to publish the case presented and for their kind assistance in the preparation of this paper.

BIBLIOGRAPHY

- ¹ Ballinger, J.: Hypoglycemia from Metastasizing Insular Carcinoma of Aberrant Pancreatic Tissue in the Liver. *Arch. Path.*, **32**, 277, 1941.
- ² Banting, F. G., and Best, C. H.: The Internal Secretion of the Pancreas. *J. Lab. and Clin. Med.*, **7**, 251, 1922.
- ³ Banting, F. G., Campbell, W. R., and Fletcher, A. A.: Further Clinical Experiences with Insulin in the Treatment of Diabetes Mellitus. *Brit. Med. Jour.*, **1**, 8, 1923.
- ⁴ Bast, T. H., Schmidt, E. R., and Sevringhaus, E. L.: Pancreatic Tumor with Hypoglycemic Status Epilepticus. *Acta Chir. Scand.*, **71**, 82, 1932.
- ⁵ Berk, J. E.: Diagnosis of Carcinoma of the Pancreas. *Arch. Int. Med.*, **68**, 525, 1941.
- ⁶ Berardinelli, W.: Hyperinsulinisme et Hypoglycémie au cours d'un Adéno-Carcinome du Pancréas. *Presse Med.*, **42**, 2098, 1934.
- ⁷ Bickel, G., Mozer, J. J., and Junet, R.: Diabète avec dénutrition grave. Disparition de la glycosuria et atténuation progressive de l'hyperglycémie à la suite du développement d'un carcinome insulaire du pancréas avec métastases hépatiques massives. *Bull. et Mem. de la Soc. Méd. des Hop. de Paris.*, **51**, 12, 1935.
- ⁸ Bru, P.: Cancer Langerhansien généralisé chez un chien. *Rev. Med.—Chir. des Maladies du Foie, du Pancréas, et de la Rate*, **2**, 40, 1927.
- ⁹ Brunschwig, A.: The Surgery of Pancreatic Tumors. C. V. Mosby Co., St. Louis, 1942.
- ¹⁰ Campbell, W. R., Graham, R. R., and Robinson, W. L.: Islet Cell Tumors of the Pancreas. *Am. J. Med. Sci.*, **198**, 445, 1939.
- ¹¹ Cannon, P. R.: Cited by Gray.²⁴
- ¹² Cecil, R. H.: Concerning Adenomata Originating from the Islands of Langerhans. *J. Exper. Med.*, **13**, 595, 1911.
- ¹³ Cottalorda, J., and Escarras.: Epithelioma Langerhansien: Extirpation, guérison. *Lyon. Chir.*, **30**, 148, 1933.
- ¹⁴ Cragg, R. W., Power, M. H., and Lindem, M. C.: Carcinoma of the Islands of Langerhans with Hypoglycemia and Hyperinsulinism. *Arch. Int. Path.*, **60**, 88, 1937.
- ¹⁵ Duff, G. L.: The Clinical and Pathological Features of Carcinoma of the Body and Tail of the Pancreas. *Bull. Johns Hopkins Hosp.*, **65**, 69, 1939.
- ¹⁶ Duff, G. L.: The Pathology of Islet Cell Tumors of the Pancreas. *Am. J. Med. Sci.*, **203**, 437, 1942.
- ¹⁷ Evangelisti, T.: Sui carcinomi pancreatici a cellule di tipo insulare. *Policlinico (sez. chir.)*, **42**, 384, 1935.
- ¹⁸ Fabozzi, S.: Über die Histogenese des primären Krebses des Pankreas. *Ziegl. Beitr. z. path. Anat. u. z. allg. Path.*, **34**, 199, 1903.
- ¹⁹ Fahri, A., and Sédad, A.: Contribution à l'étude des tumeurs malignes de la queue du pancréas. *Schweiz. Med. Wochenschrift.*, **10**, 412, 1929.
- ²⁰ Flinn, L. B., Beatty, G. A., Ginsberg, M., and Hemsath, F. A.: Carcinoma of the Islands of Langerhans with Hypoglycemia and Metastasis to the Liver. *J. A. M. A.*, **117**, 283, 1941.
- ²¹ Frantz, V. K.: Tumors of Islet Cells with Hyperinsulinism; Benign, Malignant, and Questionable. *ANNALS OF SURGERY*, **112**, 161, 1940.
- ²² Fletcher, A. A., and Campbell, W. R.: The Blood Sugar following Insulin Administration and the Symptom Complex Hypoglycemia. *J. Metab. Res.*, **2**, 637, 1922.
- ²³ Gomori, G.: Observations with Differential Stains on Human Islets of Langerhans. *Am. J. Path.*, **17**, 395, 1941, Case 4449.
- ²⁴ Gray, L. M.: Functioning Islet Cell Carcinoma with Metastases to Liver. *Am. J. Path.*, **18**, 633, 1942.
- ²⁵ Hamdi, H.: Ein Insulargenetisches Pankreascarcinom (Insulom). *Ztsch. f. Krebsforsch.*, **37**, 411, 1932.
- ²⁶ Harris, S.: Hyperinsulinism and Dysinsulinism. *J. A. M. A.*, **83**, 729, 1924.

- 27 Heiberg, K. A.: Ein Fall von Adenom in den Langerhansschen Inseln der Bauchspeicheldrüse bei einem Diabetiker. *Centralb. f. allg. Path. u. path. Anat.*, **22**, 532, 1911.
- 28 Helmholtz, H. F.: An Adenoma of Island of Langerhans. *Bull. Johns Hopkins Hosp.*, **18**, 185, 1907.
- 29 Herxheimer, G.: Über Pankreascirrhose (bei Diabetes). *Arch. f. path. Anat. u. Physiol.*, **183**, 228, 1906.
- 30 Howland, G., Campbell, W. R., Maltby, E. J., and Robinson, W. L.: Dysinsulinism: Convulsions and Coma due to Islet Cell Tumor of Pancreas: Operation and Cure. *J. A. M. A.*, **93**, 674, 1929.
- 31 Hueper, W. C.: Islet Adenoma in the Pancreas of a Mouse. *Arch. Path.*, **22**, 220, 1936.
- 32 Joachim, H., and Banowitch, M. M.: A Case of Carcinoma of the Islands of Langerhans with Hypoglycemia. *Ann. Int. Med.*, **11**, 1754, 1938.
- 33 Jacobsen, V. C.: Carcinoma of the Islets of Langerhans. *Arch. Path.*, **18**, 135, 1934.
- 34 Joslin, E. P., Root, H. F., White, P., and Marble, A.: The Treatment of Diabetes Mellitus. Lea and Febiger, Philadelphia, 1940, p. 335, Case 2.
- 35 Judd, E. S., Allan, F. N., and Rynearson, E. H.: Hyperinsulinism: Its Surgical Treatment. *J. A. M. A.*, **101**, 99, 1933.
- 36 Judd, E. S., Faust, L. S., and Dixon, R. K.: Carcinoma of the Islands of Langerhans with Metastasis to the Liver Producing Hyperinsulinism. *West. J. Surg., Obs., and Gyn.*, **42**, 555, 1934.
- 37 Keating, F. R., and Wilder, R. M.: Spontaneous Hypoglycemia: Report of Cases. *South. J. Med. and Surg.*, **103**, 125, 1941.
- 38 Kerwin, A. J.: Fatal Hyperinsulinism with Cerebral Lesions due to Pancreatic Adenoma. *Am. J. Med. Sci.*, **203**, 363, 1942.
- 39 Lang, F. J.: Über einige Geschwulstbildungen des Pankreas. *Arch. f. path. Anat. u. Physiol.*, **257**, 235, 1925.
- 40 Lloyd, P. C.: A Case of Hypophyseal Tumor with Associated Tumor-like Enlargement of the Parathyroids and Islands of Langerhans. *Bull. Johns Hopkins Hosp.*, **45**, 1, 1929.
- 41 Maximow, A. A., and Bloom, W.: A Textbook of Histology. W. B. Saunders Co., Philadelphia, 2d ed., p. 432, 1936.
- 42 Meyer, K. A., Amtman, L., and Perlman, L.: Islet Cell Tumors of the Pancreas: Report of a Case. *J. A. M. A.*, **117**, 16, 1941.
- 43 Moersch, F. P., and Kernohan, J. W.: Hypoglycemia: Neurologic and Neuropathologic Studies. *Arch. Neurol. and Psych.*, **39**, 242, 1938.
- 44 Morse, M. E.: Two Adenomata of the Islands of Langerhans. *J. A. M. A.*, **51**, 1075, 1908.
- 45 Nicholls, A. G.: Simple Adenoma of the Pancreas Arising from an Island of Langerhans. *J. Med. Research*, **8**, 385, 1902.
- 46 Pappenheimer: Cited by Whipple and Frantz.⁵⁰
- 47 Quarrier, S. S., and Bingham, C. T.: Adenoma of the Pancreas. *ANNALS OF SURGERY*, **115**, 363, 1942.
- 48 Rudd, T. N., and Walton, J.: A Case of Islet Cell Adenoma of the Pancreas. *Brit. J. Surg.*, **29**, 266, 1942.
- 49 Seckel, H. P. G.: Postmortem Hepatic Glycogenolysis in Hyperinsulinism and Glycogen Diseases. *J. Clin. Invest.*, **18**, 723, 1939, Case 195034.
- 50 Slye, M., and Wells, H. G.: Tumors of Islet Tissue with Hyperinsulinism in a Dog. *Arch. Path.*, **19**, 537, 1935.
- 51 Smith, M. G., and Seibel, M. G.: Tumors of the Islands of Langerhans and Hypoglycemia. *Am. J. Path.*, **7**, 723, 1931.

- 52 Thalhimer, W., and Murphy, F. D.: Carcinoma of the Islands of Langerhans: Hyperinsulinism and Hypoglycemia. *J. A. M. A.*, 91, 89, 1928.
- 53 Vecchio, A.: Adenoma maligno delle isole di Langerhans di un pancreas aberrante. *Arch. per le sc. med.*, 38, 277, 1914.
- 54 Warren, S.: Adenomas of the Islands of Langerhans. *Am. J. Path.*, 2, 335, 1926.
- 55 Warren, S.: The Pathology of Diabetes Mellitus. Lea and Febiger, Philadelphia, 1930, p. 181.
- 56 Wauchope, G. M.: Hypoglycemia. *Quart. J. Med.*, 2, 117, 1933.
- 57 Whipple, A. O.: The Surgical Therapy of Hyperinsulinism. *J. Internat. de Chir.*, 3, 237, 1938.
- 58 Whipple, A. O.: Present-Day Surgery of the Pancreas. *New Eng. J. Med.*, 226, 515, 1942.
- 59 Whipple, A. O., and Frantz, V. K.: Adenoma of Islet Cells with Hyperinsulinism. *ANNALS OF SURGERY*, 101, 1299, 1935.
- 60 Wilder, R. M.: Spontaneous Hypoglycemia. *Internat. Clin.*, 3, 143, 1936.
- 61 Wilder, R. M., Allan, F. N., Power, M. H., and Robertson, H. E.: Carcinoma of the Islands of the Pancreas: Hyperinsulinism and Hypoglycemia. *J. A. M. A.*, 89, 348, 1927.
- 62 Willis, R. A.: A Rare Type of Diffuse Carcinoma of the Pancreas with Unusual Metastases. *J. Path. and Bact.*, 42, 203, 1936.
- 63 Winters, W. L., Gottardo, P., and McNealy, R. W.: Severe Hypoglycemia due to Islet Adenoma of the Pancreas: Surgical Cure. *W. J. of S. G. and O.*, 49, 488, 1941.
- 64 Womack, N. A.: Hypoglycemia. *Surgery*, 2, 793, 1937.
- 65 Zanetti, G.: Contributo allo studio dei tumori del pancreas. *Arch. per le sc. med.*, 49, 505, 1927.

CHOLESTEROSIS OF THE GALLBLADDER*

OBSERVATIONS ON TWENTY-FIVE CASES WITHOUT STONES

KENNETH M. LEWIS, M.D., AND CHARLES W. PETERSON, M.D.

NEW YORK, N. Y.

FROM THE FOURTH SURGICAL DIVISION, BELLEVUE HOSPITAL, NEW YORK, N. Y.

DURING THE PAST 12 YEARS, 455 patients suffering from gallbladder disease have been operated upon on the Fourth Surgical Division at Bellevue Hospital. The cases have been studied preoperatively and followed post-operatively in a special Gallbladder Clinic. It is felt that a clinic of this type affords greater opportunity for more careful study and follow-up of these patients. In this group there were a certain number of patients whose clinical and laboratory data were not entirely conclusive, and where operation was undertaken with some indecision as to the operative findings. These latter patients frequently were found to be suffering from cholesterosis of the gallbladder, but preoperative recognition of the condition was often most difficult.

Cholesterosis of the gallbladder may be defined as a metabolic and not an inflammatory disease in which the mucosa of the gallbladder contains deposits of cholesterol and other lipid material. In the advanced stages of the disease cholesterol calculi may be present in the lumen of the gallbladder. Virchow,¹ in 1887, first noted lipid deposits in the gallbladder, and Moynihan,² in 1919, in noting yellow stippling of the gallbladder mucosa, first brought cholesterosis of the gallbladder into surgical prominence by describing it as a "condition of the gallbladder requiring cholecystectomy." MacCarty,³ in 1910, in describing the advanced stage of the disease originated the term "strawberry gallbladder," and since that time numerous authors have reported both on the clinical and research aspects of the condition. Whether the cholesterol enters the gallbladder wall from the bile (absorption), as suggested by the experiments of Illingsworth,⁴ and of Rousselot and Bauman,⁵ or from the blood (excretion), as claimed by Naunyn,⁶ and Elman and Graham,⁷ seems, clinically, to be of little consequence. The entire subject has been brought carefully up to date in the splendid analysis by Mackey,⁸ in 1937.

It is the purpose of this communication to report 25 cases of cholesterosis without stones, in which the diagnosis of a diseased gallbladder at the operating table was frequently most difficult, and to suggest an added aid in diagnosis, namely, biliary drainage, which, so far, has not been reported in the literature as a diagnostic method in the recognition of this disease. Of the 455 patients with proven gallbladder disease operated upon, 40 had cholesterosis of the gallbladder confirmed by pathologic examination. Of

* Read before The New York Surgical Society, November 25, 1942.

these 40 cases, 15 had calculi and these cases are excluded, as diagnosis at the operating table of gallbladder disease was self-evident by the palpation of calculi within the gallbladder.

In the remaining 25 cases calculi were not present, the pathology ranged from a few cholesterol plaques to a well-defined strawberry gallbladder, and diagnosis of a pathologic viscus at the time of operation by palpation and inspection of the gallbladder was extremely difficult. It is in this group that any preoperative aid in diagnosis seemed most desirable.

Of the 25 patients 20 were women and five were men, showing the large predominance of the female over the male in this condition. Eighteen of the patients were markedly obese, which would fit in well with the metabolic character of the disease. Twenty-one of the patients had complaints of indigestion, notably, flatulence, belching, epigastric distress after meals, nausea and vomiting, but the degree and number of the digestive complaints varied considerably. Three of the patients who had no symptoms of indigestion complained only of attacks of right upper quadrant colicky pain. The fourth patient who had no digestive complaints noted persistent dull aching pains in the gallbladder region but had no attacks of colic. Operation in this particular patient was postponed for almost two years, as the diagnosis of gallbladder disease did not seem certain enough to warrant surgery.

Of the 21 patients who complained of one or more of the symptoms of indigestion, 15 noted that fatty foods aggravated their symptoms, while in the remaining six, the digestive disturbances were increased by the ingestion of all types of food.

TABLE I
PREOPERATIVE SYMPTOMS—SEX—AND PHYSICAL STATUS

No. of Cases	Sex	Obese	Not Obese	Indigestion	Pain	
					Colic	Dull Aching
25	20 Females 5 Males	18	7	21	19	6

Pain was a constant factor in all of the cases, and, in analysing the group, it was surprising to note how many of the patients complained of recurrent attacks of colicky pain in the right upper quadrant of the abdomen radiating to the right scapula or right shoulder. Eighteen patients complained of frequent attacks of this type of colicky pain, one patient noted it only infrequently, and six patients complained only of a dull aching pain, with no attacks of colic. Dr. John H. Morris⁹ in a paper read before The New York Surgical Society, in May, 1934, reported on 14 cholesterosis patients, and found that attacks of biliary colic were present in 13 of the 14 cases.

Tenderness in the gallbladder region was noted in all of the patients at one or more examinations. This seemed to be a constant finding, although it was not always present at every examination. It was always noted when the patient was seen in an attack of colicky pain.

Blood cholesterol estimations were obtained preoperatively, and two to three months postoperatively, on 16 of the 25 patients. The preoperative blood cholesterol figures ranged from 125 to 235 mg. per cent, and showed such a wide divergence that no conclusions could be drawn therefrom

(Table II). Postoperatively, the blood cholesterol ranged from 125 to 180 mg. per cent, showing a definite drop in only three of the patients. It would thus seem as though blood cholesterol estimations were of little diagnostic aid, and this would conform to the findings of previous observers.

TABLE II
BLOOD CHOLESTEROL ESTIMATIONS

	No. of Cases	125-150 mg. per cent	150-175 mg. per cent	175-200 mg. per cent	200-235 mg. per cent
Preoperative.....	16	7	4	2	3
Postoperative.....	16	8	3	5	0

Cholecystographic roentgenologic studies in this series were very inconclusive. Fifteen of the patients showed diminished visualization with delayed emptying, five showed normal visualization with good emptying, and only five showed no visualization with the dye. Thus, in 20 of the patients cholecystograms were not conclusive as a diagnostic procedure. It is always difficult to evaluate a diminished or faint visualization, or to properly correlate delayed emptying by the gallbladder shadow.

It has been our custom to, preoperatively, do a biliary diagnostic drainage on all patients with suspected disease of the gallbladder. If a satisfactory drainage is not obtained at the first attempt, the drainage is repeated on one or more occasions until adequate samples of bile are secured. These samples are then allowed to stand in the icebox for from 24 to 48 hours, permitting any solid material in the bile to settle out. Microscopic examination of any sediment drawn up with a pipette is then made.

In studying the above patients with cholesterosis of the gallbladder one very frequent finding has been noted. In 19 of the 25 cases cholesterol crystals in the "B" drainage bile has been found in readily recognizable amounts. Concentrated dark green "B" bile was obtained in all of the patients, but calcium bilirubinate pigment was found in only three instances. It is extremely important that concentrated "B" bile be obtained. This is the bile contained in the gallbladder, and it is in this specimen that a search for cholesterol crystals should be made. Examination of samples of yellow bile obtained from the common bile duct may not show the crystals. If a specimen of "B" bile is not obtained at any one drainage, the drainage should be repeated at a subsequent time. It would thus seem to be suggestive that with cholesterol crystals seen in the drainage bile, and with inconclusive cholecystographic findings, a diagnosis of cholesterosis of the gallbladder might justifiably be entertained.

TABLE III
BILIARY DRAINAGE DATA

No. of Cases	Cholesterol Crystals	Calcium Bilirubinate	"B" Bile
25	19	3	25

One of the greatest difficulties in this disease has been the recognition of any real pathology of the gallbladder at the operating table. This of course applies to those cases without calculi. The gallbladder wall is thin, translucent, and not thickened. The serosa of the viscus has its normal sheen, and usually no adhesions to neighboring viscera are found. Palpation of the

CHOLESTEROSIS OF GALLBLADDER

gallbladder reveals little. It empties readily, is usually not enlarged or contracted, and thickening of the wall cannot be felt. The bluish sheen that has been described by some observers has not proved reliable in the hands of the authors. In other words, the patient has been operated upon with a preoperative diagnosis of gallbladder disease, and at the operating room table an apparently normal gallbladder is found. Nothing can be

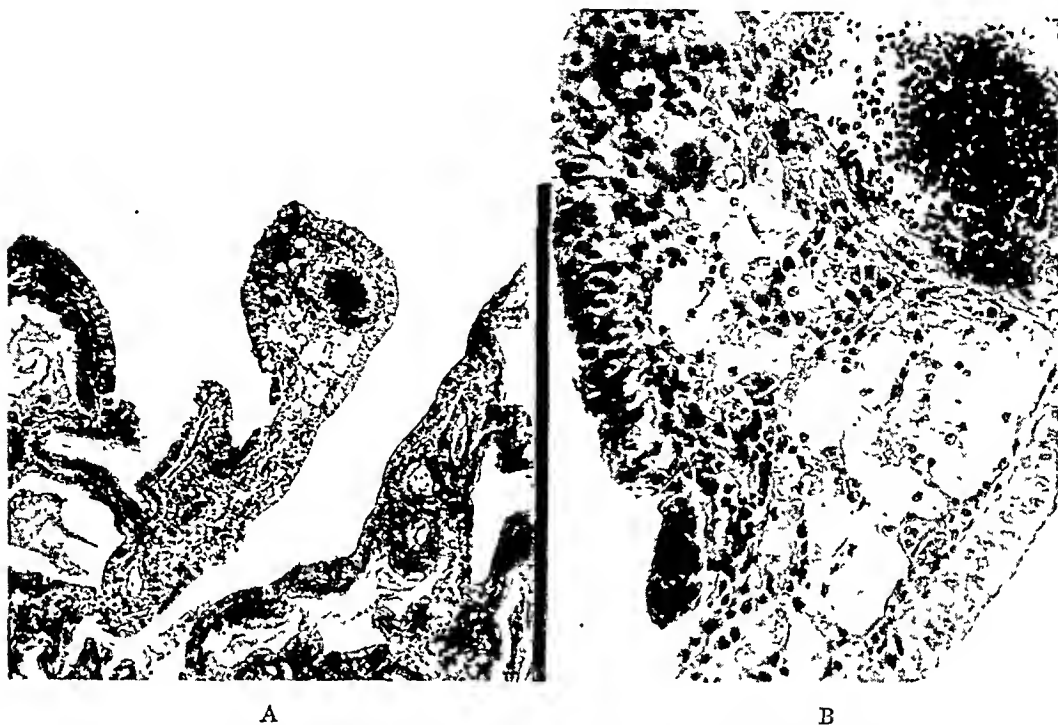


FIG. 1.—A. and B.: Cholesterosis of the Gallbladder. Note the distended, foamy cells, containing lipid in the villi of the mucous membrane. These are seen as the pale areas in the stroma. (Paraffin section: Hematoxylin-eosin—(A) Low power and (B) high power).

more disturbing than to decide whether to remove an apparently normal viscus or to leave it in. Two identical instances as described above were encountered recently. Because cholesterol crystals had been found in the preoperative drainage bile, it was decided to perform a cholecystectomy in both patients, even though the gallbladder, from the serosal surface, seemed normal. Both gallbladders, after removal, showed numerous early cholesterol and lipid deposits in the mucosa. These could be recognized grossly and were subsequently confirmed by pathologic examination.

In another instance, where, unfortunately, a preoperative biliary drainage had not been done, and where the gallbladder appeared grossly normal, it was assumed that the symptoms must be due to some other organ, and the gallbladder was not removed. Five days postoperatively the patient had a typical attack of biliary colic. Two months later a cholecystectomy was performed and a typical early cholesterosis of the gallbladder was found.

Our routine surgical procedure has been cholecystectomy, and this was performed on all of the 25 patients here reported. There was no mortality in this group, all of the patients making a satisfactory operative recovery.

We were able to follow 20 of the patients in this series. Two of these have been followed from one to two years, three from two to three years,

three from three to four years, and the remaining twelve from five to ten years. The end-results of cholecystectomy have been extremely gratifying. Of the 20 patients followed, 14 considered themselves completely cured of their previous complaints. They were able to eat all types of food with impunity and their attacks of pain disappeared. Four patients remained symptom-free as long as they stayed on a low fat diet, but otherwise had recurrence of their symptoms of indigestion. Two patients noted no improvement in their symptoms, and were unrelieved by the cholecystectomy.

It might be noted that we endeavor to keep these patients on a rigid fat-free diet for a period of six months to one year following operation. The diet is then gradually returned to a normal fat intake over a period of two to three months. The patients, if very obese, are also followed in the Obesity Clinic, where attempt is made to bring their weight somewhere near normal.

Whether rigid dietary control for some time following the cholecystectomy has played a part in relieving these patients of their symptoms, cannot, of course, be stated with certainty. In some of the patients who were observed for a number of months preoperatively, however, dietary restriction of fatty foods was insisted upon, but symptoms were never completely relieved by this alone.

TABLE IV
END-RESULTS AFTER CHOLECYSTECTOMY IN 20 CASES OF CHOLESTEROSIS, WITHOUT STONES

No. of Cases	Cured	Improved (Symptom-Free on a Low Fat Diet)	Unimproved
20	14	4	2

In reviewing the literature, one noted immediately the varying results obtained by different observers in cholesterosis gallbladder patients treated by cholecystectomy. Moynihan² considered his six patients completely cured. Illingsworth⁴ states that "treatment by cholecystectomy is the most rational procedure and appears to yield satisfactory results." Judd and Mentzer,¹⁰ commenting on 1,000 patients and cholesterosis treated by cholecystectomy at the Mayo Clinic, felt that good results only were obtained if pain had been an outstanding symptom. Young,¹¹ in 1928, reported 45 patients with strawberry gallbladders, and felt that cholecystectomy gave the most marked relief. Kopp¹² in 1929 noted that seven out of eleven cases of cholesterosis without stones were completely relieved of their symptoms by cholecystectomy. Morris⁹ reported seven cures out of the nine patients he was able to follow. Mackey,⁸ however, in a series of 33 cholesterosis cases, without stones, found only 14 cured and two improved by cholecystectomy. White and Riddick¹³ felt that cholesterosis was only a part of a general metabolic dysfunction and that cholecystectomy could not, therefore, promise relief. Stanton,¹⁴ in 1932, had four out of six cases of cholesterosis, without stones, that were not benefitted by cholecystectomy.

It can thus be seen that there is no uniformity of opinion as to the benefits of cholecystectomy in this disease, and it is extremely difficult to rationalize the divergent results obtained by so many careful and dependable observers.

It is our feeling, however, based upon our results with the group of

cases reported herein, that cholecystectomy offers relief to most of the patients with cholesterosis of the gallbladder, and this has been noted in a number of cases who have been studied and followed for a long period of time.

In contemplating surgery in this condition it should be remembered that the disease itself never causes death. Cholecystectomy, on the other hand, is accompanied by a certain risk if the number of patients operated upon is large enough. Each patient should, therefore, be carefully observed and cholecystectomy should be reserved for those cases in whom the symptoms are so severe as to warrant surgical intervention. It is probable that a certain number of patients with this disease never progress to calculus formation. In our series, 15 out of 40 cases did have calculi. It is our impression that the number of cholelithiasis patients with accompanying cholesterosis of the gallbladder wall is probably greater than has previously been thought. Pathologic sections should be taken from different areas of all removed gallbladders, as there may be areas of cholesterosis and chronic cholecystitis in the same gallbladder. This has been noted several times in our series.

SUMMARY

1. Twenty-five cases of cholesterosis of the gallbladder without stones, treated by cholecystectomy, are reported. Twenty of these patients were followed, postoperatively, for from one to ten years.

2. Pain was a predominant symptom in this group, and 19 of the patients complained of recurrent attacks of typical biliary colic in the upper abdomen.

3. Cholecystograms were inconclusive, only five of the cases showing non-visualization of the gallbladder.

4. Preoperative diagnostic biliary drainage revealed cholesterol crystals in the bile in 19 of the cases. This procedure is urged as a diagnostic aid in this disease, where frequently the signs, symptoms and roentgenologic findings may be so indefinite.

5. In our series cholecystectomy gave satisfactory results. Of the 20 patients whom we were able to follow, 14 were relieved of all symptoms, four were relieved as long as they stayed on a low fat diet, while two patients were unimproved.

REFERENCES

- ¹ Virchow, R.: *Virchow's Arch.*, 2, 574, 1857.
- ² Moynihan, B. G. A.: *ANNALS OF SURGERY*, 50, 1265, 1909.
- ³ MacCarty, W. C.: *ANNALS OF SURGERY*, 51, 651, 1910.
- ⁴ Illingsworth, C. F. W.: *Brit. Jour. Surg.*, 17, 203, 1929.
- ⁵ Rousselot, L. M., and Bauman, L.: *Surg. Gynec. & Obst.*, 61, 585, 1934.
- ⁶ Naunyn, B.: *Die Entstehung u. d. Aufbau. d. Gallensteine*, 1923, Jena.
- ⁷ Elman, R., and Graham, E. A.: *Arch. of Surg.*, 24, 14, 1932.
- ⁸ Mackey, W. A.: *Brit. Jour. Surg.*, 24, 570, 1937.
- ⁹ Morris, J. H.: Paper read before the New York Surgical Society, May, 1934.
- ¹⁰ Judd, E. S., and Mentzer, S. H.: *Collected Papers of the Mayo Clinic*, 19, 310, 1927.
- ¹¹ Young, E. L.: *New Eng. Jour. Med.*, 198, 729, 1928.
- ¹² Kopp, J. G.: *Arch. f. Klin. Chir.*, 151, 411, 1928.
- ¹³ White, C. S., and Riddick, A. L.: *Southern Med. Jour.*, 21, 857, 1928.
- ¹⁴ Stanton, E.: *Am. Jour. Surg.*, 18, N.S., 246, 1932.
- ¹⁵ Boyd, W.: *Brit. Jour. Surg.*, 10, 337, 1922-3.

LATE INVASION OF BLADDER AND PROSTATE IN CANCER OF THE RECTUM OR RECTOSIGMOID FOLLOWING ABDOMINO-PERINEAL RESECTION*

GORDON D. OPPENHEIMER, M.D

NEW YORK, N. Y.

FROM THE UROLOGIC AND SURGICAL SERVICES OF THE MT. SINAI HOSPITAL, NEW YORK, N. Y.

THIS STUDY was undertaken after a successful palliative urologic procedure had been performed upon a patient with recurrence of the tumor in the prostate and bladder neck seven years after an abdomino-perineal resection for cancer of the rectum. Eight additional instances of late postoperative lower urinary tract recurrence were found in the recent hospital records and form the basis of this report. Two of these nine cases were operated upon at other institutions. Three were ward cases and four were private patients operated upon by three different surgeons.

Until recently this type of case was not seen by our Urologic Service. Apparently, when vesical neck obstruction and hematuria became prominent symptoms, the patient was considered hopeless and referred for chronic institutional care. However, with improvement in the mortality rates of radical extirpation of the rectum, and with the increase in the total number of operations performed, more patients are living following the procedure, resulting in a greater interest and attention directed to the postoperative complications and sequelae.¹ Postoperative difficulties in micturition due to disturbed neurogenic vesical control and other factors have been noted and studied by many workers. We, as have others, have obtained satisfactory results in relieving bladder stasis by transurethral resection of minimal vesical neck obstruction in this type of vesical detrusor weakness. There have been several such cases in the last three years. True prostatic fibro-adenomatous obstruction has not infrequently become symptomatic after abdomino-perineal resection and has been cured similarly by transurethral resection. It is because of these good results that cases with urinary symptoms have been referred to the urologic surgeon, thus affording us the opportunity of seeing patients who had late neoplastic infiltration of the bladder and prostate.

Because of the close anatomic relationship between rectum or lower sigmoid colon and the lower urinary tract, direct involvement of the latter by the lower bowel cancer theoretically should occur with some frequency. In an "acute hospital" such as Mt. Sinai we do not see many cases presenting the terminal stages of cancer of the rectum. Through the courtesy of Dr. D. Marine, Chief of the Laboratory Division of the Montefiore Hospital, New York City, I reviewed 50 consecutive recent

* Read before the New York Surgical Society, January 27, 1943.

autopsy protocols from that hospital in which cancer of the rectum was one of the diagnoses. Ten of these patients (six females and four males) had an abdomino-perineal or a posterior resection. Of the males, one patient had involvement of bladder, prostate and seminal vesicles, and in another, prostate and seminal vesicles were infiltrated. Four of the six females had bladder involvement. The forty other patients had either no operation or palliative colostomy. Some had received radiotherapy without apparent effect. Thirteen were females and four of these had bladder involvement. Twenty-seven in this "nonextirpative" group were males. Fourteen of these, or a little over 50 per cent, had invasion by the growth of bladder, or prostate or seminal vesicles either separately or together. Twelve of the 14 had bladder involvement. Briefly, of 50 autopsied patients who were cared for in the last stages of their disease (20 per cent had a rectal resection) there was invasion of the bladder in 21 cases. Three patients in the unoperated group had rectovesical fistulae, and one a rectovaginal fistula. The end-picture of the cases with bladder involvement was essentially the same whether the rectum had been extirpated or not, namely the picture of a "frozen" pelvis. Bladder, prostate and seminal vesicle involvement in the male, and bladder and uterine involvement in the female, apparently takes place by direct extension.

Although well known, and previously reported,² the fact that these patients very frequently died from upper urinary tract complications, was forcibly brought to my attention by the study of these necropsies. Six of the ten cases with rectal extirpation, and 16 of the remaining 40 inoperable cases, making a total of 22 cases out of the 50, or 44 per cent, showed evidences of compression of one or both ureters in the pelvis with or without direct invasion. Most times direct invasion was not present. Several other patients had true ureteral metastases. As a result of the ureteral compression, dilatation of the ureter, renal pelvis and calices was present, often with infection, and evidence of pyelonephritis, and sometimes with multiple renal abscesses, and even perinephric suppuration. Upper urinary tract infection was either a direct or contributing cause of death in a considerable proportion of these cases. In fact, it seemed that the mortality from ureteral blockage, with renal damage and infection, would have been even greater except that some of these patients died as result of complications associated with their metastases or, rarely, from localized infection associated directly with the primary lesion. Incidentally, 33 of the 50 cases (66 per cent) had metastases; these were usually multiple.

In general, my findings are similar to those of Kickham and Bruce,² who, reporting from a hospital devoted entirely to the care of cancer patients, analyzed a postmortem group of 88 cases of cancer of the rectum, clinically inoperable, in whom no extirpative surgery was performed. Seventy per cent of these cases were males, and in 31.5 per cent of the males, some cancerous invasion of the prostate could be demonstrated. Forty per cent

of the entire group showed vesical involvement. Rectovesical fistulae were noted in two cases. Forty-seven point seven per cent of the 88 cases showed occlusion of one or both ureters by actual compression or direct invasion, with resulting hydronephrosis, pyelonephritis and advanced renal damage. Incidentally, renal metastases were found in two of their patients.

Metastasis to the lower urinary tract as one of multiple metastases theoretically may occur. Solitary metastasis to the bladder must be very rare, but if present in an accessible location may be successfully treated by surgical means. As judged by the postmortem findings mentioned above, all the evidence indicates that residual cancer with subsequent contiguous direct extension accounts for the late malignant involvement of the bladder, prostate, or seminal vesicles under consideration. One might state that the more advanced the primary rectal tumor is in its local growth, the greater is the likelihood that the patient will have secondary invasion of the bladder or prostate following the extirpation.

The following report is probably typical of many of the cases who are operated upon for a locally advanced lesion.

ILLUSTRATIVE CASE REPORTS

Case 1.—Hospital No. 447541: J. Z., a 49-year-old male, entered the Mt. Sinai Hospital, February 27, 1939, and was discharged, April 12, 1939. He had suffered from bilateral apical pulmonary tuberculosis 25 years before. He complained of blood in the stool for one year, with increasing frequency of defecation, rectal tenesmus and loss of weight. The report of the biopsy specimen taken from a fungating cauliflower rectal mass was infiltrating adenocarcinoma. On March 6, 1939, a one-stage abdominoperineal resection was performed. No intra-abdominal metastases were found but there was considerable fixation to the prostate. The specimen showed a circumscribed tumor, about 3.5 cm. in diameter and about 3 cm. above the anal margin, which grossly infiltrated all coats of the rectum and invaded the perirectal fat. The pathologic report was "ulcerative infiltrating adenocarcinoma of rectum. Invasion of perirectal tissue. No involved lymph nodes were found." The patient was well for three months, gained weight, but then began to complain of dysuria, frequency, and back pain. Roentgenograms of the dorsolumbar spine were negative for metastases. Six months after operation he complained of the same symptoms, with an episode of hematuria. A short course of radiotherapy was given, but perineal, back and bladder pain with frequency and nocturia continued. Because of a stricture at the site of colostomy, the colostomy was revised. He finally was admitted to the Montefiore Hospital, December 28, 1939, and died, March 29, 1940, about one year after the original operation. The postmortem findings were as follows:

Autopsy.—Local recurrence of carcinoma of the rectum, with invasion of pelvic tissues, pubic bones, bladder, prostate and seminal vesicles and with metastases to the liver, ureters, vertebrae, regional and celiac lymph nodes. Bilateral ureteropyelonephrosis, with suppurative pyelonephritis. Chronic fibroid pulmonary tuberculosis, with cavitation. Bilateral bronchopneumonia. Bronchiectasis upper lobes. Chronic cystitis, with incrustations.

Comment: The patient was operated upon one year after symptoms had commenced. Undoubtedly, cancer cells were left on the posterior aspect of the prostate and bladder and in the perirectal lymphatics and fat. Local

recurrence and involvement of the lower urinary tract became apparent. No surgical or urologic therapy could have been of any value. He died with metastases, urosepsis, and terminal bronchopneumonia.

Contrasted with this is the unusual case mentioned in the introduction of this paper.



FIG 1.—Cystogram. Small diverticulated bladder on right side of pelvis. Bladder elevated above pubis. Normal lower end of ureters visualized by excretory urogram.

Case 2.—Hospital No. 477773: H. A., a 66-year-old man, was admitted to the Mt Sinai Hospital, August 16, 1941, and discharged, August 26, 1941. Seven years previously, August 17, 1934, a one-stage combined abdomino-perineal resection had been performed. (Dr. D. Jones, Palmer Memorial Hospital, Boston, Mass.) The growth was annular, started about 12 cm. above the anus and was 2.5 cm. wide. It was situated above the peritoneum, which covered a very deep rectovesical pouch. The neoplasm penetrated the entire wall of the bowel and had grown through the peritoneum on the anterior surface. There were nodules on the adjacent peritoneum, and the tumor had apparently extended through to involve the seminal vesicles. There were no liver metastases. At the second part of the operation, when the ischiorectal fat, sphincter, rectum and growth were removed from below, the surgeon commented on the technical difficulty because of the seminal vesicle involvement. The seminal vesicles were removed with the tumor and the bowel. The pathologic report was "malignant adenoma, with metastases to one lymph node." Grossly, the seminal vesicles were infiltrated by tumor tissue. The prognosis was considered poor. The patient was given radiotherapy by Dr. J. R. Freid, of this city. Two years after operation, a hard, fixed mass developed in the right lower quadrant of the abdomen but disappeared after intensive radiotherapy.* He was well until eight months before admission to this

* Details of Radiotherapy (Dr. J. R. Freid). From 1/18/35 to 2/1/35, and from 5/16/35 to 6/7/35, eleven small X-ray treatments, totaling 1800 r. high voltage to perineal sinus. 7/19/37 to 8/20/37, treated over 15x14 cm, anterior and posterior right lower pelvic portals, each of these areas receiving 3000 r. Factors were 200 K V, Thorius filter (equal to 2 mm. Cu.) 80 cm. T.S.D.

institution, when he suffered from gradually increasing frequency of urination and burning on urination. Examination revealed a fair state of nutrition, but some evidence of weight loss, a well functioning colostomy to the left of the umbilicus, a satisfactory perineal scar, and systolic cardiac murmurs at the aortic and mitral areas. The residual urine was six ounces. The urine contained pus and *B. coli*. Blood urea nitrogen was 10 mg. per 100 cc. An excretory urogram showed normal excretion on both sides, without dilatation of the pelves, calices or ureters. The latter were visualized to the bladder. The cystogram (Fig. 1) indicated a diverticulated bladder, which

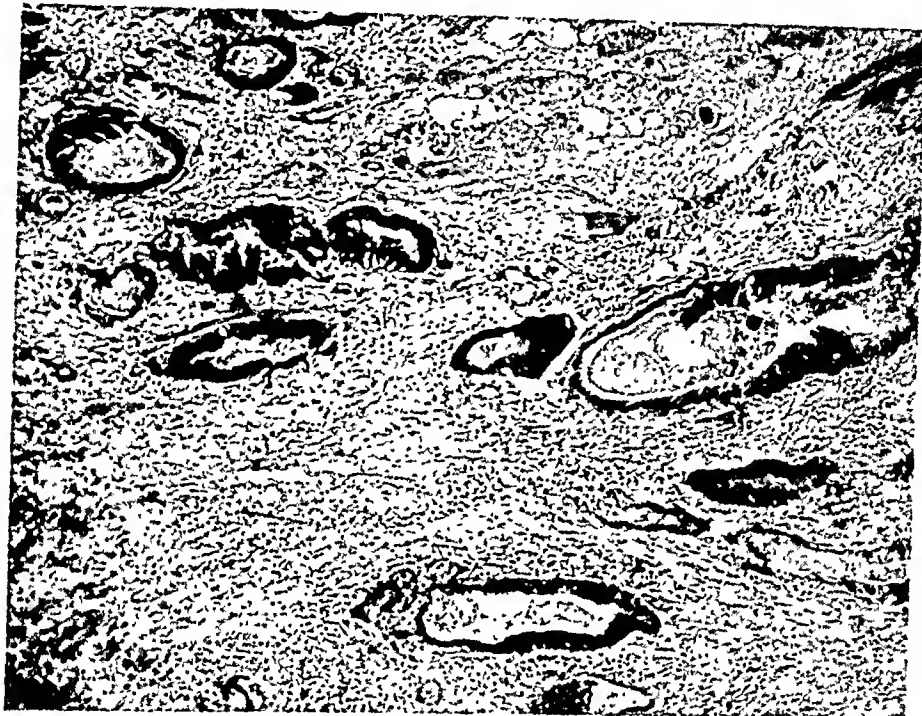


FIG. 2.—Photomicrograph of transurethraly resected tissue showing infiltrating adenocarcinoma similar to original rectal carcinoma.

appeared to be fixed to the right side of the pelvis. A preliminary bilateral vas transection was performed. On August 8, 1941, under low spinal anesthesia, a cystoscopy and transurethral resection were performed. The bladder was trabeculated. There was intra-urethral lateral lobe encroachment both in the midline and superiorly. The inferior vesical sphincter was elevated. On the left side some of the resected tissue was spongy and different from the right side. Fifteen grams of tissue were removed. The patient was discharged five days later, voiding well, without residual. The pathologic report (Dr. P. Klemperer) was adenocarcinoma infiltrating the prostate (Fig. 2). A comparison with a slide of the original specimen led Dr. Klemperer to state that they were quite identical histologically, and that the cancer in the transurethraly resected tissue was definitely secondary to direct extension from residual rectal growth. He received further very intensive high voltage radiotherapy,* and was well up to November, 1942 (15 months), except for a short episode of urinary frequency and burning, with pyuria, which promptly responded to sulfadiazine therapy. There was no residual urine.

* From 9/2/41 to 11/4/41, treated over five fields: right and left pubic, right and left gluteal, and perineal portal. He received 2500 r. to each of these areas. Other factors were 200 K.V., filtration 0.5 mm. Cu. plus 3 mm. Al., 80 cm. T.S.D.

On November 16, 1942 (eight years and three months after abdomino-perineal resection) the patient was readmitted to the Mt. Sinai Hospital because of recurrent urinary frequency, dysuria, urgency, and pyuria. A large vesical calculus was seen roentgenologically (Fig. 3). The excretory urogram, again, indicated a normal upper urinary tract, and, again, the bladder (Fig. 4) was situated on the right side of the pelvis but showed no prostatic intrusion. Under spinal anesthesia, the stone was crushed and evacuated. The vesical outlet and prostatic urethra presented only a very small amount of intruding tissue—from this area three grams of tissue were removed with the McCarthy resectoscope, for biopsy. Much to my surprise, none of this tissue showed any evidence of cancerous infiltration. The serum "acid" phosphatase was four King-Armstrong units. The patient was discharged several days later, and has been well since.



FIG. 3.—Large vesical calculus. Two smaller shadows are outside of bladder.

Comment: Histologically, the original rectal tumor and the infiltrating neoplasm affecting the prostate were similar. Biologically, however, this tumor is unusual because it is very slow growing and evidently radiosensitive. The result obtained justifies our frequent attempts to undertake radical surgery even though the local lesion is fixed to surrounding structures and also justifies later palliative therapeutic efforts.

Case 3.—Hospital No. 484107: B. W., a 49-year-old physician, had three admissions to the Mt. Sinai Hospital, the first in May, 1941. His past urologic history was that of right renal colic in 1911, and, in 1917, colic with the spontaneous passage of a stone. Four years before admission, a one-stage abdomino-perineal resection with a left iliac colostomy had been performed at another institution for a cancer of the rectosigmoid. He had been well until shortly before admission, when frequency, dysuria, loin pain, and painless hematuria developed. Cystoscopy showed a solid spher-

ical-shaped neoplasm about the size of a hickory nut on the trigone, to the left of the right ureter orifice and extending towards the left lateral wall. The pathologic report of the biopsy was "fragments of adenocarcinoma." On May 20, 1941, an exploratory celiotomy was performed (Dr. A. Hyman). The peritoneum was free of metastases. The liver and pelvic region showed no gross evidence of neoplasm. The bladder was mobilized and opened in the midline. A flat necrotic growth, the size of a quarter, was found in the bladder, overlying the right ureter orifice and extending close to the sphincter. The base of the bladder was indurated. The tumor was treated by the introduction of 12 platinum radon seeds of 0.75 millicuries each, placed circularly around the periphery and center of the growth. Suprapubic Malecot catheter drainage was established. One month later, the tumor was fulgurated transurethrally. The supra-



FIG. 4.—Cystogram Bladder on right side of pelvis, but no prostatic intrusion effects seen

pubic wound healed, but a few months later, cystoscopy revealed viable tumor tissue at the site of the original vesical tumor. The tumor was thoroughly fulgurated and six additional radon seeds were introduced transcystoscopically. Two months later, the patient again had urinary frequency, urgency and hematuria, with infected urine, and five ounces of residual urine. Recurrent tumor was seen, and also median prostatic lobe hypertrophy. The tumor was fulgurated and transurethral resection of the prostate was performed, January 7, 1942. The clinical course was progressively downhill. He died in March, 1942, five years after the original abdomino-perineal resection, and ten months after discovery of the bladder tumor. There was no necropsy.

Comment: The findings at exploratory celiotomy might indicate that the bladder lesion was a solitary local recurrence or metastasis. This, of course, would be most unusual. The surgeon had proposed total cystectomy, with ureteral implantation into the skin, but the patient had refused.

Case 4.—Hospital No. 461544: L. S., was a 33 year-old man, with symptoms of rectal bleeding, weight loss, and sense of mass in rectum, for at least four months.

A typical abdomino-perineal resection was performed, August 16, 1939, for a low rectal tumor. The rectum was very adherent to prostate, seminal vesicles and membranous urethra. The pathologic report was "infiltrating adenocarcinoma of rectum. Adjacent lymphatics show carcinomatous involvement." One year later, he was readmitted to the hospital for frequency and difficulty in urination, and attacks of acute retention. Cystometric studies showed a slightly hypotonic curve. The residual urine was 18 ounces. On intravenous pyelography, a normal right upper urinary tract, with incomplete filling on the left side, was found. Cystoscopy showed lateral lobe intrusion and some bar formation. Following cystoscopy he had an attack of acute pyelonephritis and a *B. proteus* bacteremia. On September 26, 1940, a transurethral resection was performed. The pathologic report was "fragments of prostatic tissue and bladder showing infiltrating adenocarcinoma identical with that of previously resected adenocarcinoma of the rectum." The patient's urinary symptoms improved, and he was discharged to the Dept. of Radiotherapy, but received only four treatments. He died at a municipal institution four months later (one and one-half years after the rectal resection). The cause of death was given as "metastases" to bladder and prostate, chronic pyelonephritis, and uremia.

Comment: This is another typical case illustrating bladder and prostatic involvement after rectal resection, with death from upper urinary tract infection, *etc.*, probably due to ureteral obstruction by recurrent neoplasm in the pelvis.

Case 5.—Hospital No. 477854: H. W., was a 53-year-old male, with a six-month history, who presented himself to the Mt. Sinai Hospital, September 11, 1940, with a tumor of the rectum near the prostate. The biopsy showed "infiltrating colloid adenocarcinoma." An abdomino-perineal resection was performed. The convalescence was uneventful except for a temporary urinary leak from an operative perforation of the urethra. The extirpated specimen showed lymph node metastases. Seven months later, the patient was cystoscoped because of frequency, dysuria and pyuria. The cystoscopist thought that only an acute cystitis was present, but he biopsied a small posterior vesical wall protrusion. This showed "fragments of bladder mucosa and mucus cell carcinoma." No treatment was given. The patient entered the Montefiore Hospital, August 26, 1941, and died, February 8, 1942 (17 months after the original operation). The necropsy diagnoses were: Recurrent colloid carcinoma, with invasion of bladder, prostate, seminal vesicles, and innominate bone, and pressure on great vessels of pelvis. Metastases to the mesenteric lymph nodes, testis, epididymis and left adrenal. Compression of the right ureter by tumor tissue, with pyoureter, pyelonephritis, and perinephritis. Congenital absence of left kidney. Acute splenic tumor. Some parenchymatous degeneration of viscera. Congestion and edema of lungs.

Comment: From the postmortem findings, it does not appear likely that any of our known therapeutic aids could have helped this patient. However, at the time of the late postoperative cystoscopy, the perineal wound was still open. I think radium might have been applied to the bladder and pelvis through this wound, in an attempt to check the local recurrence although I do not know of any case helped in this way.

Case 6.—Hospital No. 407608: M. C., a 55-year-old woman, was operated upon December 30, 1935. A one-stage abdomino-perineal resection was performed. The tumor was three inches above the anus and infiltrated the rectal wall. The report was adenocarcinoma with lymph node metastasis. The patient developed severe perineal and back pain and, after 16 months, showed an extensive invasion of the whole pelvis

and bladder. Thoracic chordotomy was performed, resulting in some relief of the pain. The patient died 19 months after the original operation.

Case 7.—Hospital No. 433675, D. E., was a 41-year-old man with symptoms of four months duration. He had a large ulcerating mass in the ampulla of the rectum. On December 6, 1934, a parasacral resection of the rectum, with preservation of the sphincter and restoration in continuity, was performed. The pathologic report was adenocarcinoma with one lymph node involved. The entire specimen measured 6 x 8 cm., and was occupied by an annular carcinoma with normal rectum 6 mm. on either side. The tumor, grossly, infiltrated all coats and perirectal fat. The patient was well for three and one-third years, when pelvic pain and constipation developed. At the site of anastomosis, a recurrent cancer was found and confirmed by biopsy. On April 18, 1938, an abdomino-parineal resection with permanent sigmoid colostomy was performed. The liver was free of metastases. The rectum was adherent to the concavity of the sacrum, and the recurrent rectal cancer involved the prostrate, necessitating removal of the posterior aspect of the prostate and capsule. The histologic report showed adenocarcinoma in the rectal submucosa and prostatic tissue, with one involved lymph node. Patient's recovery was satisfactory, but eight months later patient entered hospital with symptoms of recurrent profuse urinary bleeding. The intravenous pyelogram showed bilateral upper urinary tract dilatation. Cystoscopy showed cancerous invasion of the base of the bladder. He died five and one-half years after the first operation, from repeated attacks of severe vesical hematuria. There was no postmortem.

Comment: Although the same postoperative sequelae often follow initial radical resection, partial resection with preservation of the anal sphincter is considered an inadequate procedure for this disease. Certainly, the patient stands a better chance against local residual cancer with later active recurrent growth in the pelvis if the initial operation is wide and complete.

Case 8.—Hospital No. 487704: N. S. was a 48-year-old male, with symptoms of rectal bleeding for several months due to a cancer palpable 5 cm. above the anal margin. On September 14, 1936, a first-stage Lahey operation was performed. No metastases were present. On October 3, 1936, the second-stage combined operation was undertaken. The tumor measured 6 x 4 x 2 cm. The pathologic report was "adenocarcinoma." The specimen was prepared by the oil of wintergreen method, but none of nine lymph nodes which were found showed metastatic involvement. The postoperative convalescence was uneventful. Approximately 15 months later (January 24, 1938) the patient was readmitted because of right loin pain, fever, and hematuria. The urologic study indicated a normal left upper urinary tract, and a functioning infected hydroureteronephrosis on the right side. A right ureteronephrectomy was performed. The kidney, histologically, showed evidence of acute and chronic pyelonephritis and ureteritis. The patient was readmitted to the hospital, May 9, 1941, about five years after the original resection because of difficulty in voiding, burning, nocturia and hematuria. Cystoscopy showed a large solid neoplasm on the floor of the bladder. The neoplasm was biopsied and fulgurated. Histologically, the biopsy showed fragments of bladder wall infiltrated by adenocarcinoma. The patient was discharged two weeks after admission. On October 22, 1941, a large papillary neoplasm was seen cystoscopically on the right side of the floor of the bladder overlying the right ureter orifice. This was again fulgurated. Later, because of severe right loin pain, a chordotomy was performed at the Neurological Institute. On the fourth admission (January 4 to 12, 1942) vesical neck obstructive symptoms were present, with a residual urine of 16 ounces. On cystoscopy, three calculi were seen on the floor of the bladder. At the site of the previously treated tumor, there was some irregular elevation of the

mucosa. The stones were crushed, and three grams of tissue were resected from the inferior sphincter. No evidence of malignancy was found. He left the hospital voiding without difficulty. The fifth admission was terminated by the patient's death, May 18, 1942, about six years after the two-stage resection. He had evidences then of diffuse metastases, particularly in the liver. The picture was one of gradual deterioration with increasing bladder irritability. There was no postmortem examination.

Comment: Although not proved, local residual recurrent cancer around the right ureter at the bladder may have led to the early infected right hydro-ureteronephrosis. The tumor was slow growing, and vesical involvement did not become pronounced until three and one-half years later. Even if radical extirpation of the bladder had been performed, this probably would not have influenced the development of hepatic metastases.

Case 9.—Hospital No. 483687: J. S., a 40-year-old male, was admitted to the Mt. Sinai Hospital, April 6, 1941, and a one-stage abdomino-perineal resection was performed on the day of admission. The tumor was situated about 2.5 cm. from the anus; perirectal tissues were indurated, and the left seminal vesicle was adherent to the rectum. The pathologic report was "infiltrating adenocarcinoma of the rectum, with involvement of many lymph nodes." About six months after discharge, dysuria, pyuria and complete urinary retention was found to be due to irregular intrusion of tissue at the vesical neck. A transurethral resection was carried out, December 27, 1941. The histologic report was "fragments of prostatic tissue infiltrated by adenocarcinoma." Comparison of the slides of the rectal carcinoma and the resected prostatic tissue led Doctor Klemperer to the conclusion that the prostatic cancerous infiltration was secondary to the rectal cancer. Because of persistent urinary symptoms, including some incontinence, the patient entered the Urologic Service of one of the city hospitals. Here, another transurethral prostatic resection was performed, and the report of the removed tissue was adenocarcinoma of the prostate. A bilateral orchidectomy was performed, February 13, 1942, and a permanent suprapubic cystotomy established, March 14, 1942, for persistent urinary difficulty. He was admitted to the Montefiore Hospital, April 12, 1942. The serum "acid" phosphatase was 3.6 King-Armstrong units. Although no metastases were found on admission, he later developed cord compression from upper cervical vertebral metastases and died, October 6, 1942, one and one-half years after the rectal extirpation. A limited necropsy was done. The anatomic diagnoses were as follows: Adenocarcinoma infiltrating prostate, with direct extension to bladder wall, pelvic soft tissues and left ischium. Right pyonephrosis and perinephric abscess. Right and left pyoureter. Right and left pyelonephritis. Subacute cystitis. Acute splenic tumor.

Comment: This case offered considerable difficulty in determining the primary site of the cancer, inasmuch, as the autopsy findings could be interpreted either as a primary cancer of the rectum or prostate. No prostatic tissue could be recognized either grossly or microscopically in the dense scar-like tumor masses which occupied the pelvis. In view of the definite surgical diagnosis of cancer of the rectum, and particularly the age of the patient (41 years), cancer of the rectum seemed the more probable. A review and comparison of all the surgical and autopsy material from the three hospitals was made, which led to the conclusion that the slides from the resected rectum, prostate, and autopsy were histologically similar and, in view of all the evidence, a final diagnosis of primary cancer of rectum

was made. The importance of differential diagnosis is based on the possible therapeutic efficacy of orchidectomy in cancer of the prostate, as originally advocated by Huggins.³ For future cases, two possible aids are suggested to distinguish between primary cancer of the prostate and secondary cancer of the prostate from a primary rectal cancer. The first is the serum acid phosphatase determination.⁴ Primary prostatic cancer with metastases usually gives an elevated serum acid phosphatase, while in primary rectal cancer with or without prostatic involvement, the determination should be normal.⁵ A second histologic aid may be in the use of a new staining method of transurethrally resected prostatic tissue. This method, described by Gomori,⁶ demonstrates acid phosphatase activity in tissue sections. Prostatic cancer which contains large amounts of acid phosphatase stains strongly positive, as compared with a rectal cancer infiltrating the prostate gland which should, on the information at hand, not stain heavily. However, further studies will have to be made on these suggested laboratory aids.

While on the subject of prostatic cancer, attention should be called to the fact that the differential diagnosis between it and a low, anterior wall, primary rectal cancer may be difficult. Kickham and Bruce² mention four cases of prostatic cancer simulating rectal cancer in which the presenting symptoms were rectal. We have had several similar experiences.

Concerning the frequency of this sequela of lower urinary tract malignant infiltration following abdomino-perineal resection, I cannot give exact figures from our material. There have been no recently published statistics from this institution relating to the follow-up observations of the operative cases of carcinoma of the rectum. One of the reasons is that the grouping of these cases has changed hands several times, so that not enough time has elapsed for a proper evaluation. A recent study⁷ of the immediate results of the surgical treatment of cancer of the rectum on the wards of the hospital for a four-year period showed that 85 patients were subjected to operation. Fifty-one were operable. In 36 cases, a one-stage abdomino-perineal resection was carried out, with six deaths, or an operative mortality of 16.6 per cent. In the remaining 15 operable cases, various other procedures were undertaken. The three ward cases, which have been detailed above, are from the group of 30 patients who survived the one-stage abdomino-perineal resection. Therefore, in this group the incidence of late involvement of bladder, prostate or seminal vesicles would be at least 10 per cent. However, our figures are too small to be reliable. Ewert⁸ analyzed the urologic complications in 452 cases of extirpation of the rectum. The rectal lesion initially involved the ureter in 11 cases, the bladder in 23 cases, and the prostate in 19 cases. He states that in five patients in whom rectal resection was done, the growth invaded the prostate after operation, producing obstruction which required bladder neck resection. However, the number of cases followed postoperatively, or the length of follow-up is not mentioned.

It is outside of the scope of this communication to discuss in detail the

urinary complications of surgically treated or untreated cancer of the rectum or sigmoid. The literature on this subject is ample. From a urologic viewpoint, however, it is worth remembering, as pointed out by Schwartz and Bergman,⁹ that urinary symptoms believed to be due to a lesion in the urinary tract are not infrequently secondary to a primary lesion in adjacent bowel, either neoplastic or inflammatory.

SUMMARY

Nine instances of late invasion of the bladder and/or prostate and seminal vesicles following abdomino-perineal resection for cancer of the rectum or recto-sigmoid are reported. The management of these cases is described. One of the patients appears to have been remarkably helped by radiotherapy and transurethral resection. The sequelae under discussion may occur more often than formerly realized. Upper urinary tract complications are found very frequently in the later stages of cancer of the lower bowel. Although cancerous invasion of the lower urinary tract after abdomino-perineal resection appears to render the situation hopeless palliative urologic or surgical measures and radiation therapy should often be attempted, with the expectation of prolonging life.

REFERENCES

- ¹ Jones, T. E.: Complications of One-Stage Abdomino-Perineal Resection of Rectum. J. A. M. A., **120**, 104-106, September, 1942.
- ² Kickham, C. J. E., and Bruce, N. H.: Urological Complications in Malignant Disease of the Rectum. Journal of Urology, **41**, 541-556, April, 1939.
- ³ Huggins, C., Stevens, R. E., Jr., and Hodges, C. V.: Studies on Prostatic Carcinoma; II. The Effects of Castration on Advanced Carcinoma of the Prostate Gland. Archives of Surgery, **43**, 209-233, August, 1941.
- ⁴ Sullivan, T. J., Gutman, B., and Gutman, A. B.: Theory and Application of the Serum "Acid" Phosphatase Determination in Metastasizing Prostatic Carcinoma: Early Effects of Castration. Journal of Urology, **48**, 426-458, October, 1942.
- ⁵ Gutman, A. B.: Personal communication.
- ⁶ Gomori, G.: Distribution of Acid Phosphatase in the Tissues under Normal and Pathologic Conditions. Archives Pathology, **32**, 189-199, August, 1941.
- ⁷ Garlock, J. H., Ginzburg, L. and Glass, A.: Complications and Causes of Mortality of the Surgical Treatment of Carcinoma of the Colon and Rectum. To be published.
- ⁸ Ewert, E. E.: A Comparative Analysis of the Urological Complications following Large Bowel Surgery. Journal of Urology, **46**, 764-776, October, 1941.
- ⁹ Schwartz, J., and Bergman, H.: Urologic Aspects of Carcinoma of the Colon and Rectum. Urological and Cutaneous Review, **41**, 3-7, 1937.

COCHLIOMYIA AMERICANA INFESTATION IN MAN

CASE REPORT

R. O. PEARMAN, M.D., AND L. HASEMAN, Ph.D.*

ST. JOSEPH, MO.

COCHLIOMYIA AMERICANA C. and P. is the name given to the New World screw-worm fly by Cushing and Patton¹ to separate this dangerous form, which feeds on the tissues of living animals, from the blowfly (*Cochliomyia macellaria*) which is more particularly a scavenger fly.

The screw-worm fly is native to the warmer sections of the Americas, but on its own power or by the movement of infested animals may spread into the "corn belt," to cause serious damage to livestock and other warm-blooded animals, including man. The adult fly may readily be mistaken for a medium-sized blowfly. It has a deep greenish-blue metallic color with yellow, orange or reddish face, and three dark stripes on the dorsal surface of the thorax. Unlike the blowfly, however, it is normally attracted to fresh cuts or bloody wounds rather than to purulent sores. Its larvae bore into and destroy the healthy tissue surrounding the wound, which may prepare the wound for a subsequent attack by the common blowflies. On livestock, wire cuts, dehorning wounds, castration cuts, navel wounds, and other skin injuries are the usual sources of screw-worm entrance. On man, entrance occurs most commonly through the ears, nostrils or exposed surface wounds, usually while the individual is asleep or unconscious.

In the last few years, the screw-worm fly has been of increasing importance as a pest of livestock in the Middle West. While, presumably, it is unable to withstand the winters, new infestations have been established each summer by the shipment of infested animals from the south and by the northward migration of the adult flies. In 1941, the pest spread from centers of introduction so as to cover entire counties and involve hundreds of animals. With frosts coming so late, as in the last two open falls, the pest has been able to continue to breed later than usual, so as to attack animals and man throughout October. In southern California,² this menace is present the year round, being more prevalent in the late fall and winter.

Along with this increase of its importance to livestock has developed its real menace to man. Any untreated cut, scratch, blister, insect bite, or other raw wound on the surface or any irritation in the nostrils, ears and eyes of man or beast may serve as an attraction to the fly. The female fly may deposit a few hundred eggs at the rate of 60 per minute, and with the eggs hatching in about a day, an untreated wound may soon become heavily infested with maggots. The young worms promptly begin to penetrate and destroy the tissues, eating in by means of the powerful oral hoods, and causing

* Professor of Entomology, University of Missouri, Columbia, Mo.

a burning, pinching type of pain, characteristic urine-colored discharge, and a most disagreeable odor. The maggots may become full-fed in four to a maximum of ten days. The adult worms drop out of the wound, bury in the ground, and after a week in the pupa stage emerge as a fly which soon mates and more eggs are deposited. This means that several broods of the pest may develop during the summer months.

Wallace³ states that there appears to be a slight rotary motion as the worms busy themselves with their destructive feeding, and that their motility is due to the circular spines around their bodies, which are similar to the thread on screws, and from which they get their characteristic name.

Literature^{3, 4, 5, 6} dealing with the screw-worm fly refers to various cases of infestation in man. Most of these cases were undoubtedly screw-worm infestations, although the maggots were rarely saved and identified as those of the screw-worm fly by experts in this field.



FIG. 1.—Patient after the removal of the larvae. Note the gangrenous area lateral to the right nostril.

August 12, 1941, one of us (R. O. P.) removed 80 apparently full-fed maggots from a lesion of the cheek of an elderly woman, which were identified by C. T. Greene, D. G. Hall, and later by E. F. Knipling,⁷ Federal authority on screw-worm infestation, as definitely the larvae of the screw-worm fly, *Cochliomyia americana* C. and P.

Case Report.—D. M., age 58, married, was admitted to St. Joseph Hospital, August 11, 1941, with what, at first, appeared to be an abscess of the right side of her face. She said that she had been bitten on the right cheek, five days before admission to the hospital, by a spider or fly. The following day the right side of her face itched and became swollen and painful. The swelling became larger and the pain increased in intensity; and the night before admission to the hospital she coughed up a larva, and developed a bloody discharge from the nose and mouth. Ten hours

before admission, she noticed a gangrenous area about the size of a dime at the site of what she thought to be the original bite.

Physical examination was essentially negative except for a marked swelling of the right side of her face surmounted by a gangrenous area 1.5 cm. in diameter, and located 1.75 cm. lateral to the right nostril. Temperature 101° F., pulse 90, respirations 20. W.B.C. 11,350, neutrophile 80%, lymphocytes 20%. R.B.C. 3,250,000, hemoglobin (Sali) 61%, blood Wassermann positive. Roentgenologic examination of sinuses: Both maxillary and right anterior ethmoid sinuses were moderately cloudy—not dense, but sufficient to indicate pathologic residue. Chest: Negative.

The patient was anesthetized with intravenous pentothal sodium, the nose and right cheek were painted with tincture of methiolate. The lesion was opened through the gangrenous area by means of a hemostat. A few larvae were obtained, accompanied



FIG. 2.—A few of the larvae obtained ($\times 12$). They were so active that several crawled out of the photographic field before the picture could be taken.

by approximately an ounce of foul smelling serosanguineous discharge. Upon further exploration of the lesion, many more larvae were observed spreading out in a fan-shaped manner and burrowing into the ragged, bloody and somewhat honeycombed tissue at the periphery of the lesion. These larvae were removed individually with a thumb forcep (Fig. 1). A total of 80 larvae were removed from the lesion. The ragged lining of the resulting cavity was curetted away down to healthy appearing tissue. The cavity was noted to open into the right nasal passage, and the nasal septum was perforated. The maxilla was roughened, but the process had not broken into the right maxillary sinus. The curettings and several pieces of tissue from the edge of the opening were saved for pathologic diagnosis. The cavity was swabbed out with tincture of methiolate and packed with vaselined gauze *Pathologic Report:* Inflammatory tissue.

Most of the larvae were preserved in alcohol, although a few were kept in hopes that adult flies might emerge, but they failed to do so. The larvae were very active, of the usual maggot shape, 12 to 15 mm. in length and 2 to 2.5 mm. in diameter (Fig. 2), and gray-white in color with a tint of reddish-brown due to the tissue exudate which filled their intestinal tracts. The larva had 12 body segments, each of which was encircled by a narrow ring of minute spines, giving the larva the resemblance to

a screw. The head of the larva was rather pointed and was provided with an oral hood surmounted by two hook-like projections. The larger end of the larva was provided with two brownish plates through which it is supposed to breathe.

A volatile poison such as chloroform or benzol will kill the larvae and aid in their removal, especially in inaccessible lesions. However, in this case, the use of such an agent was not necessary.

The patient was discharged, August 19, 1941, markedly improved. Two months later, the area was completely healed and the patient appeared normal. No antiluetic therapy had been given in the interim, because the patient refused to come back to the clinic for treatment.

The patient lives in a poor and very unsanitary part of the city, about a mile from the stockyards and packing houses. The house opens directly onto the sidewalk and is a dark shack crowded between two similar houses. The windows were not screened, but the front entrance had an old, dilapidated screen door. The backyard was low, littered with trash and overgrown with weeds. At the time she was supposed to have been bitten by an insect, the hide of a butchered goat hung in the coal house, and the place was alive with flies. She also reported flies in the house. She stated that she did not take naps in the daytime, and that she did not have any sores or scratches on her face nor any nasal discharge at the time of the supposed bite.

Those of us who saw the case were of the opinion that the fly must have deposited its eggs in her right nasal cavity, and that the maggots worked out from there to form the lesion in the cheek. This would seem to be the logical explanation; for if there were no breaks in the skin on the cheek, the fly must have laid its eggs in the patient's right nostril. The fly probably gained access to the house, and in the early morning while the patient slept, deposited the eggs in her nostril, where perhaps unknown to her she may have had some irritation. Then the supposed spider or insect bite on the cheek was probably merely pain due to the first activity of the young maggots, some five days before they were removed at operation.

COMMENTS

(1) With the spread of the screw-worm infestation among cattle, more cases in humans may be expected in the near future.

(2) Maggots from any wound should always be saved for identification by an entomologist.

(3) Wounds should always be kept covered to protect them from flies.

(4) Persons afflicted with sores about, or discharges from, the aural or nasal cavities should sleep only in well-screened houses, and should keep the areas protected from possible attack by flies when outside.

(5) A volatile poison (chloroform or benzol) will kill the larvae and aid in their removal, especially from inaccessible lesions.

REFERENCES

- ⁱ Cushing, E. C., and Patton, W. S.: Studies on the Higher Diptera of Medical and Veterinary Importance. *Cochliomyia Americana*, the Screw-worm Fly of the New World. *Ann. Trop. Med. and Parasitol.*, 27, No. 4, 539-551, November, 1933.

- ² McCapes, A. M.: California Polytechnic College, San Luis Obispo, Calif. Personal communication.
- ³ Wallace, W. R.: Screw-worm Infestation: (Case Report). J. South Carolina M. A., 32, 213-215, September, 1936.
- ⁴ Craig, C. F., and Faust, E. C.: Clinical Parasitology, Philadelphia, Lea and Febiger, 1940, p. 613.
- ⁵ Turnbull, F. M., and Franklin, L. B.: Aural Infestation with Screw-worms. J. A. M. A., 120, 117-119, September 12, 1942.
- ⁶ Knipling, E. F., and Rainwater, J. T.: Species and Incidence of Dipterous Larvae Concerned in Wound Myiasis. J. Parasitol., 23, 451-455, October, 1937.
- ⁷ Knipling, E. F.: Dept. of Entomology, Bureau of Agriculture, Washington, D. C. Personal communication.

BRIEF COMMUNICATIONS



UMBILICAL DISCHARGE IN ACUTE APPENDICITIS

REPORT OF TWO CASES

PHILIP D. ALLEN, M.D., AND ROBERT A. JOHNSON, M.D.

NEW YORK, N. Y.

FROM THE CHILDREN'S SURGICAL SERVICE, BELLEVUE HOSPITAL, NEW YORK, N. Y.

INVOLVEMENT of the umbilicus secondary to inflammatory disease of the appendix is uncommon. Cullen,¹ in his treatise on the diseases of the umbilicus, states that he has never seen this structure involved in appendicitis.

Umbilical discharge may occur as the result of spontaneous rupture of an appendiceal abscess resulting in an entero-umbilical fistula or it may result from a generalized peritonitis secondary to inflammation of the appendix. A case will be presented illustrating each of these two conditions.

Purulent drainage from the umbilicus secondary to a generalized peritonitis has been reported by many writers, including Heurtaux,² Vaussy,³ and Gauderon.⁴ The peritonitis in most instances has been classified as idiopathic. The pneumococcus was the most frequent organism found, and the condition occurred most often in young females. Haggard⁵ reported umbilical discharge occurring in a case of peritonitis in which the clinical signs indicated acute appendicitis as the basic pathologic process, but this was not proved by operation or autopsy.

Case 1.—Hosp. No. 194701: R. S., white, female, age two and one-half years, was admitted to the hospital, August 14, 1941, with a history that five days before she had had an upper respiratory infection, anorexia, vomiting and abdominal pain. Three days after onset the child had two generalized convulsions and was referred on the fifth day to Willard Parker, a hospital for contagious diseases, with a tentative diagnosis of meningitis. She was at once transferred to Bellevue Hospital, with a diagnosis of perforated appendix and spreading peritonitis.

On admission, the child was in a prostrate condition, with a temperature of 103° F., pulse 124, respirations 40. Positive physical findings were limited to the abdomen, which was markedly distended, with moderate tenderness throughout. No masses were palpable. Rectal examination revealed induration but no definite mass.

The white blood count was 9,500, with 75 per cent polymorphonuclear leukocytes, 24 per cent lymphocytes, and 1 per cent monocytes. There was 1+ albumen in the urine. The hematocrit was 44, and the plasma protein 5.5 grams.

Supportive therapy consisting of small blood transfusions, oxygen and sulfonamides were given. Clinically, the child improved, and on the fifth hospital day the temperature was 100° F., pulse 110, white blood count 14,150. Two days later thick, creamy pus began to drain from the umbilicus in small amounts. Under local anesthesia, a McBurney incision was made and a large amount of thick, purulent material was evacuated from the peritoneal cavity. Drains were inserted without further exploration and the wound was packed open with vaselined gauze. A right lower lobe pneumonia

developed postoperatively, and purulent material continued to drain from the umbilicus and the operative wound. The patient expired on the seventh postoperative day.

Necropsy.—Limited to the abdomen. The peritoneal cavity was the site of a purulent plastic peritonitis. There were numerous loculated abscesses one of which, in the region of the umbilicus, contained several hundred cubic centimeters of yellowish-green pus. Examination of the bowel revealed that the cecum opened into the free peritoneal cavity through the eroded opening of the appendiceal stump. The remainder of the appendix was not found.



FIG. 1.—Roentgenogram showing the lipiodal visualization of the umbilical sinus

The drainage of an appendiceal abscess through the umbilicus with the establishment of an entero-umbilical fistula has been reported in the literature by Kelly and Hurdon,⁶ Vaussy,³ Bryant and Hime.⁷ These case reports present clinical histories which would seem to implicate the appendix, but operative or autopsy evidence is lacking.

Case 2*.—Hosp. No. 37410-42: L. B., white, female, age four, was admitted to Bellevue Hospital, July 9, 1942, with the chief complaint of discharge from the umbilicus, of one week's duration. The mother stated that 15 days prior to admission the child had had a transitory attack of abdominal pain, without vomiting or disten-

* Presented before the New York Surgical Society, November 11, 1942.

bance of bowel habit. This brief episode did not force the child to go to bed, and she continued to play about in the usual manner.

Physical examination was negative except for the umbilicus, in the center of which was a small pouting area presenting an opening about five millimeters in diameter. The surrounding skin was eroded and the discharge was yellowish-green in color, without fecal odor. The abdomen was soft, without tenderness, spasm or palpable mass. Rectal examination revealed a small mass at the tip of the examining finger.

The temperature was 99° F., on admission. The white blood count was 7,200, with 70 per cent polymorphonuclear leukocytes, and 30 per cent lymphocytes. Gross and microscopic examination of the urine was negative. Examination of the discharge for free hydrochloric acid was negative. Twenty cubic centimeters of methylene blue was injected into the tract, but none appeared in the urine. Ten cubic centimeters of lipiodol was then injected into the tract and roentgenograms visualized the terminal ileum, cecum and ascending colon (Fig. 1). A diagnosis of Meckel's diverticulum, with a patent fistulous opening through the umbilicus was made, and operation was performed on the fifth hospital day.

Operation.—Through a right rectus muscle-splitting incision, a firm mass, covered with omentum, was found to be attached to the anterior abdominal wall about five centimeters below the level of the umbilicus. On dissecting free the omentum there was found to be encapsulated in it a sloughing appendix. The cecum was identified and the base of the appendix transected, the stump inverted, and what remained of the appendix was removed in a retrograde fashion. The fistulous tract leading to the umbilicus was laid open, curetted, and packed with vaselined gauze.

The postoperative course was uneventful. The opened sinus tract healed in slowly from below, and was entirely healed when the child was discharged on the twentieth postoperative day.

The pathologic laboratory confirmed the diagnosis of acute and chronic inflammation of the appendix.

SUMMARY

These two case reports have been presented, with the operative and autopsy findings, to illustrate the uncommon occurrence of umbilical discharge secondary to inflammatory disease of the appendix. This may occur either as the result of generalized peritonitis of appendiceal origin, as illustrated by Case 1, or by the spontaneous drainage of an appendiceal abscess, with the formation of an entero-umbilical fistula, as in Case 2.

REFERENCES

- 1 Cullen, T. S.: *The Umbilicus and Its Diseases*. W. B. Saunders Co., Philadelphia, p. 296, 1916.
- 2 Heurtaux, A.: *Phlegmon sous ombilical*. Bull. et Mein de la Soc. de Chir. de Paris n. s., 3, 641, 1877.
- 3 Vaussy, F.: *Des phlegmons sous peritoneaux de la paroi abdominale anterieur*. These de Paris, No. 445, 1875.
- 4 Gauderon, A. D.: *De la peritonite idiopathique aigue des enfants de sa terminaison par suppuration et par evacuation du pus a travers l'umbilic*. These de Paris, No. 148, 1876.
- 5 Haggard, W. D.: Quoted by Cullen, T. S.¹; *The Umbilicus and Its Diseases*. W. B. Saunders Co., Philadelphia, p. 305, 1916.
- 6 Kelly and Hurdon: *The Vermiform Appendix and Its Diseases*. 1905. p. 202. W. B. Saunders Co., Philadelphia.
- 7 Bryant and Hine: *Medical Times and Gaz.*, 2, 460, 1878.

SPONTANEOUS RUPTURE OF A NORMAL SPLEEN

CASE REPORT

CAPTAIN ANGUS D. McLACHLIN, R.C.A.M.C.

TORONTO, CANADA

FROM THE DEPARTMENT OF SURGERY, UNIVERSITY OF TORONTO, AND SURGICAL SERVICE, TORONTO GENERAL HOSPITAL, TORONTO, CANADA

THE NORMAL SPLEEN is not uncommonly ruptured by trauma. On occasion, the loss of blood at time of injury may be slight because the laceration is speedily occluded by a thrombus. In some instances this thrombus may proceed to healing by fibrosis. In other cases it may be detached by further injury or may soften and be freed spontaneously. A second and much more severe intraperitoneal hemorrhage may then take place. Jackson¹ recorded a case of this type in which the severe hemorrhage occurred 28 days after the initial injury. The term "exploding spleen" has been coined to describe this second phenomenon. A review of the early literature on traumatic rupture of the normal spleen and of the history of splenectomy was made by Barnes.²

Preexisting disease of the spleen is a strong factor in determining rupture by trauma. A blow to an abdomen containing a large, friable malarial spleen might well result in a fatal hemorrhage from that organ, a fact taken advantage of by ingenious assassins of the middle ages.

Susman³ found record of spontaneous rupture of the spleen in malaria, typhoid, pregnancy, parturition and the puerperium, leukemia, hemophilia, acute infections, tuberculosis, and even more rarely in typhus fever, relapsing fever, cystic degeneration, malignant growth, hydatid disease, infarction, torsion, abscess and varices.

Spontaneous rupture of an apparently normal spleen is much less frequent. Zuckerman and Jacobi⁴ collected 20 genuine and seven doubtful instances in the period prior to 1937. Since then, Dudgeon⁵ has contributed another case. Recent European journals have contained articles on the subject, but are not available on this continent. The purpose of this report is to present another example of spontaneous rupture of an apparently normal spleen.

Case Report.—B. K., male, age 46, lumberjack, suffered from generalized crampy abdominal pain with nausea and vomiting and some tenderness in the right lower abdomen for one week, a year prior to admission. He received no medical attention at that time, and on recovery felt entirely well until one week before coming into the hospital. During that week he developed symptoms suggestive of a subacute intestinal obstruction. Physical examination on admission was in accordance. There was no abdominal rigidity or tenderness, and no masses could be made out. On roentgenologic examination, the plain films revealed moderately distended loops of small bowel, and the barium enema showed a fixed and irregular terminal ileum, suggestive of an inflammatory disease. The distension cleared up rapidly after admission, and he re-

mained in bed, with no complaints, and with no elevation of temperature, increased pulse rate or unusual W.B.C. count.

Twelve days after admission, without premonitory symptoms, he developed sudden, severe generalized abdominal pain, followed in a few moments by pain behind the left shoulder tip. The pain was increased by any shifting of his body. On examination, he appeared acutely ill, with ashen color and clammy skin. The abdomen was slightly distended and uniformly tender. There was uniform guarding of the abdominal wall, but not true board-like rigidity. Free fluid was easily demonstrated, but Ballances' test was not attempted. The abdomen was silent. Rectal examination revealed extreme tenderness high up, but was not otherwise helpful. There was no free air in the abdominal cavity demonstrable roentgenologically. The pulse was 130; B.P. 80/60; temperature 99.2° F. per rectum; and W.B.C. 23,000.

After administration of morphine, 250 cc. of plasma, and 600 cc. of whole blood, the general condition of the patient improved sufficiently to make celiotomy feasible. The abdominal cavity was entered through a short midparamedian incision on the right side. Bloody fluid and blood clots presented immediately. A rapid manual examination revealed that there were more blood clots in the left upper abdomen than elsewhere. The incision was extended upward, and the spleen delivered into the wound. The splenic capsule had been stripped up and split open, and there was blood clot adherent to the splenic pulp. The vessels were ligated separately at the hilum and the spleen removed. The liver was normal in size, color and consistency. There were adhesions between loops of small intestine in the lower abdomen, but further exploration did not seem warranted at this time. About 1500 cc. of blood clot and another 100 cc. of bloody fluid was removed from the peritoneal cavity; the wound was closed without drainage; and the patient returned to bed to an oxygen tent. Recovery was free from complications. The hemoglobin was 33 per cent the day following operation, with an admission level of 80 per cent. The platelet count was 473,000 at five days, and still 410,000 two weeks after operation. Blood smear, differential W.B.C., and van den Bergh level were normal, and the Wassermann was negative.

Because of the still undiagnosed lesion in the lower abdomen, the abdominal cavity was opened again five weeks after the splenectomy. The small bowel "tie-up" was found due to a former acute appendicitis. This was straightened out and the appendix removed. Convalescence was once again uneventful.

Pathologic Report: This specimen consists of a small, markedly contracted, relatively avascular spleen, which measures 8 x 6 x 3.5 cm. On the diaphragmatic surface of the spleen the capsule has been stripped up by an effusion of blood. Portions of blood clot are still adherent to the outer part of the splenic pulp. Sections of the spleen reveal it to be firm and contracted, and liver-like in consistency, almost no blood exuding from the cut surface. The malpighian corpuscles and trabeculae are difficult to make out. Serial gross sections of the spleen fail to reveal any infarct or other area of softening to account for the subcapsular hemorrhage. The vessels at the hilum of the spleen fail to reveal any abnormality. No traumatized area, and no zone definitely identifiable as the site from which the hemorrhage occurred is present.

Microscopic sections of this spleen fail to reveal any information as to the mechanism resulting in the extensive subcapsular hemorrhage. The spleen is markedly contracted, so that the sinusoids and the other vascular channels contain almost no blood. The arterioles are thickened throughout. The trabeculae appear normal. The capsule, where stripped up, shows a slight chronic inflammatory infiltration of lymphocytes.

Discussion.—The correct diagnosis was not reached before operation. A proven lesion at the terminal ileum made it seem the most likely source of the general peritoneal irritation. The development of pain in the left shoulder

tip soon after onset of the general abdominal pain suggested that the accident had occurred in the upper abdomen. The short midabdominal incision, capable of extension in either direction, was an admission of this uncertainty in diagnosis.

The clinical findings were not entirely in keeping with perforation of a hollow viscus. The fall in blood pressure and rise in pulse rate seemed out of proportion to the other clinical findings and might have suggested that blood loss played a part in the picture. Free fluid was demonstrated both by transmission of fluid wave and by shifting dullness. Ballance's sign was not tried, and might have solved the problem.

The cause of a spontaneous hemorrhage from an apparently normal spleen is difficult to explain. In the absence of a rent in the splenic pulp it seems likely that the initial hemorrhage was between the splenic pulp and the capsule. A logical sequence of events would then be a gradual elevation of the splenic capsule, rupture of the capsule and then massive intraperitoneal bleeding following on the relief of pressure. No blood clot of any age was found, and a slight chronic inflammatory infiltration of lymphocytes in the stripped up splenic capsule is the only evidence that the whole process did not occur in rapid order.

The etiology of the initial hemorrhage is even more perplexing. A minor blow to the abdomen just sufficient to rupture a small vessel deep to the capsule and initiate the process is an attractive theory. In opposition to this, the patient had been confined strictly to bed for 12 days prior to the accident, and had been very quiet during the preceeding week. On careful questioning he could recall no blow to the abdominal wall during the previous several months that had been severe enough to be remembered.

Susman³ noted that vague gastro-intestinal symptoms were sometimes present in the period before rupture of a normal spleen. He believed that congestion of the portal vein and its radicals might force blood between the splenic pulp and capsule and finally force the latter to give way. The period of subacute intestinal obstruction immediately before rupture in this case could well have produced a portal congestion. In contradiction of this theory, spontaneous rupture of the spleen has not been reported in portal cirrhosis or thrombosis, where portal congestion should be much more severe.

Wohl⁶ observed that the malpighian bodies and capsule of the spleen showed thickening and hyaline changes at a comparatively early age. He considered that spontaneous rupture of the apparently normal spleen was due to a local degeneration in the wall of a blood vessel. In the case presented here the arterioles were thickened, but these changes seemed within the normal range.

Perisplenic adhesions which fixed the spleen in position might, conceivably, predispose to injury, but were not present here.

In conclusion, no definite cause can be assigned to this spontaneous rupture of an apparently normal spleen. Its occurrence soon after an episode

of subacute intestinal obstruction is some evidence that venous congestion might play a rôle in the etiology.

SUMMARY

1. A case of spontaneous rupture of an apparently normal spleen is presented.

2. There was no tear in the splenic pulp, and a subcapsular hematoma, with stripping of the splenic capsule and final rupture into the peritoneal cavity, seemed the likely sequence of events.

3. No adequate cause for the hemorrhage was found, but the accident occurred during convalescence from a subacute intestinal obstruction, and is some evidence that venous congestion may play a rôle in the initial hemorrhage.

I wish to thank Dr. Roscoe R. Graham for permission to publish this case and Professor W. L. Robinson for the pathologic report.

REFERENCES

- ¹ Jackson, T. S.: Rupture of the Spleen: Report of an Unusual Case. *Surg. Gynec. & Obst.*, **41**, 331-332, September, 1925.
- ² Barnes, A. F.: Subcutaneous Traumatic Rupture of the Normal Spleen. *ANNALS OF SURGERY*, **59**, 597-609, 1914.
- ³ Susman, M. P.: Spontaneous Rupture of Spleen. *Br. Jour. Surg.*, **15**, 47-54, July, 1927.
- ⁴ Zuckerman, I. C., and Jacobi, M.: Spontaneous Rupture of Normal Spleen. *Arch. Surg.*, **34**, 917-928, May, 1937.
- ⁵ Dudgeon, H.: Spontaneous Rupture of Spleen. *South. Med. Jour.*, **34**, 1247-1249, December, 1941.
- ⁶ Wohl, M. C.: Spontaneous Rupture of Spleen. *ANNALS OF SURGERY*, **82**, 246-249, August, 1925.

BOOKS RECEIVED

FIRST AID SURGICAL AND MEDICAL. By Warren H. Cole, M.D., and Charles B. Puestow, M.D., M.S., Ph.D. New York: D. Appleton-Century Company, Inc., 1942.

SYNOPSIS OF TRAUMATIC INJURIES OF THE FACE AND JAWS. By Douglas B. Parker, M.D., D.D.S. St. Louis: C. V. Mosby Co., 1942.

TRAUMATIC SURGERY OF THE JAWS. By Kurt H. Thoma, M.D. St. Louis: C. V. Mosby Co., 1942.

THE TIME OF MY LIFE. By Harry Carlos De Vighne, M.D. Philadelphia and New York: J. B. Lippincott Co., 1942.

LYMPH NODE METASTASES. By Grantley Walder Taylor, A.B., M.D., F.A.C.S., and Ira Theodore Nathanson, M.S., M.D. New York: Oxford University Press, Inc., 1942.

TRANSACTIONS OF THE SOUTHERN SURGICAL ASSOCIATION, FIFTY-FOURTH ANNUAL MEETING. Edited by Alton Ochsner, M.D. Philadelphia and New York: J. B. Lippincott Co., 1941.

RELIGION AND HEALTH. By Seward Hiltner. New York: Macmillan Co., 1943.

MANUAL OF OXYGEN THERAPY TECHNIQUES. By Albert H. Andrews, Jr., M.D. Chicago: The Year Book Publishers, Inc., 1943.

ATLAS OF OVARIAN TUMORS. By Gemma Barzilai, M.D. New York: Grune and Stratton, 1943.

TRANSACTIONS OF THE SIXTY-THIRD MEETING OF THE AMERICAN SURGICAL ASSOCIATION. Edited by Walter Estell Lee, M.D. Philadelphia and New York: J. B. Lippincott Co., 1942.

TREATMENT OF FRACTURES. By Guy A. Caldwell, M.D., F.A.C.S. New York and London, Eng.: Paul B. Hoeber, Inc., Medical Book Department of Harper Brothers.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.

ANNALS OF SURGERY

VOL. 117

APRIL, 1943

No. 4



RESTORATION OF BLOOD FLOW IN DAMAGED ARTERIES

FURTHER STUDIES ON A NONSUTURE METHOD OF BLOOD VESSEL ANASTOMOSIS

ARTHUR H. BLAKEMORE, M.D., JERE W. LORD, JR., M.D.,

AND

PAUL L. STEFKO

NEW YORK, N. Y.

FROM THE DEPARTMENTS OF SURGERY, PRESBYTERIAN HOSPITAL, COLUMBIA UNIVERSITY, COLLEGE OF PHYSICIAN AND SURGEONS, AND THE NEW YORK HOSPITAL, CORNELL UNIVERSITY MEDICAL COLLEGE, NEW YORK, N. Y.

THERE WERE 4,403 U. S. soldiers who lost one or more extremities¹ during the last World War, and of this number only 13 per cent (690)² lost their limbs in battle. Of the remaining 3,713 cases, surgical amputation was resorted to. The majority of these surgical amputations were performed because of infection or because of the presence of serious damage to the blood supply, or both. Attempts at suture of severed arteries was "by-and-large" unsuccessful and, therefore, considered impractical.^{3, 4, 5}

Perhaps reflecting the improved methods of treating wounded extremities in the present war, a recent British war memorandum by Admiral G. Gordon-Taylor, and his associates,⁶ has the following to say regarding amputation: "The main indication for amputation is irreparable interference with blood supply. No matter how severe the destruction of skin, comminution of bones or contamination of tissues, if the main blood vessels are not destroyed, the limb can usually be saved."

We postulate in this war that the use of the sulfonamides in conjunction with careful débridement, careful hemostasis with the evacuation of blood clot will, for the first time in the history of wars, enable the surgeon to safely postpone amputation in cases of ligated primary arteries until the true status of the collateral circulation is established. Furthermore, such measures, perhaps in conjunction with the use of anticoagulants, will afford the basis for success of a simple, nonsuture method of arterial anastomosis.

* Presented before the Combined Meeting of the Philadelphia Academy of Surgery, and the New York Surgical Societies, at the Academy of Medicine, New York, February 10, 1943.

The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development, and the Cornell Medical College.

We should like to report our experience using the vitallium* tube, or tubes, as a prosthesis for blood vessel anastomosis.

METHODS

Several different technics (Figs. 1, A and B, and 2 A) were attempted before a satisfactory method was discovered. In brief, the suture of the divided carotid (or femoral) artery over a vitallium tube was successful

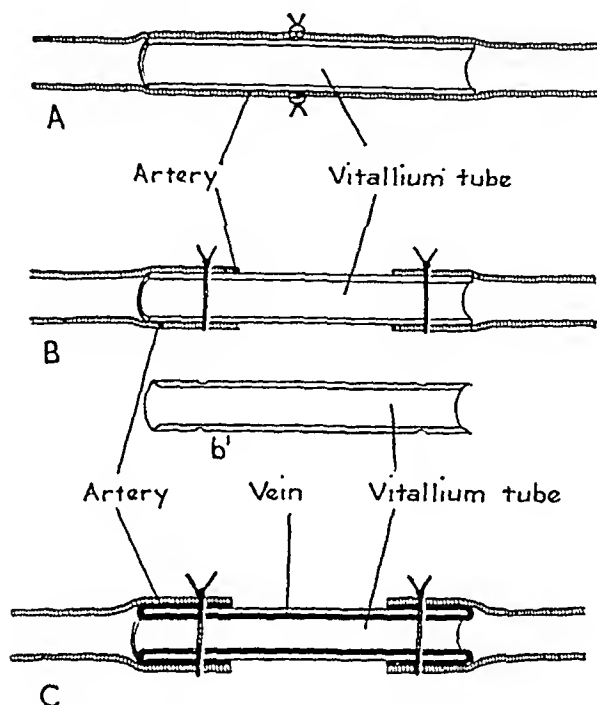


FIG. 1.—In these drawings are depicted the different methods of using a single vitallium tube. (A) The artery is sutured in the usual manner over a straight vitallium tube. (B) The divided ends of the artery are approximated near each end of the vitallium tube by ligatures, in this way a gap is bridged. (C) The final technic which was highly successful. The drawing shows the vein to be inside the vitallium tube; the ends of the vein are everted over the vitallium tube, and the artery is drawn over each end and held by a ligature. In this way the flowing blood contacts only an intimal-lined tube.

in only one out of nine experiments, and in the successful one blood flow was demonstrated for only five days (Fig. 1 A). Bridging a gap with a vitallium tube by the ligature technic (Fig. 1 B) was also most disappointing (none out of six). Finally, the bringing of each end of the divided artery through a vitallium tube and bridging the gap with a vein transplant was successful in only two cases out of seven (Fig. 2 A).

After the above failures, a technic was established of bridging a gap in an artery which functioned fairly well in the small femoral artery and with

* The approximate composition of vitallium is cobalt 65%, chromium 30%, and molybdenum 5%. The tubes were supplied by the Austenal Laboratories, Inc., of Chicago and New York. We wish to thank Mr. J. J. Erdmann of that company for his cooperation.

NONSTUTURE ARTERIAL ANASTOMOSIS

uniform success in the abdominal aorta for an indefinite length of time (Figs. 1 C and 2 C). Dogs have been used as the experimental animals, and silk technic was used throughout. No anticoagulant was employed. Vitallium tubes 2.5 cm. long, with an outer diameter of 3 Mm. and an inner diameter of 2 Mm., have been used as a permanent prosthesis for a vein transplant. The operation (Fig. 3) is carried out as follows: The femoral artery and vein of the dog are located and isolated for distances of 7 to

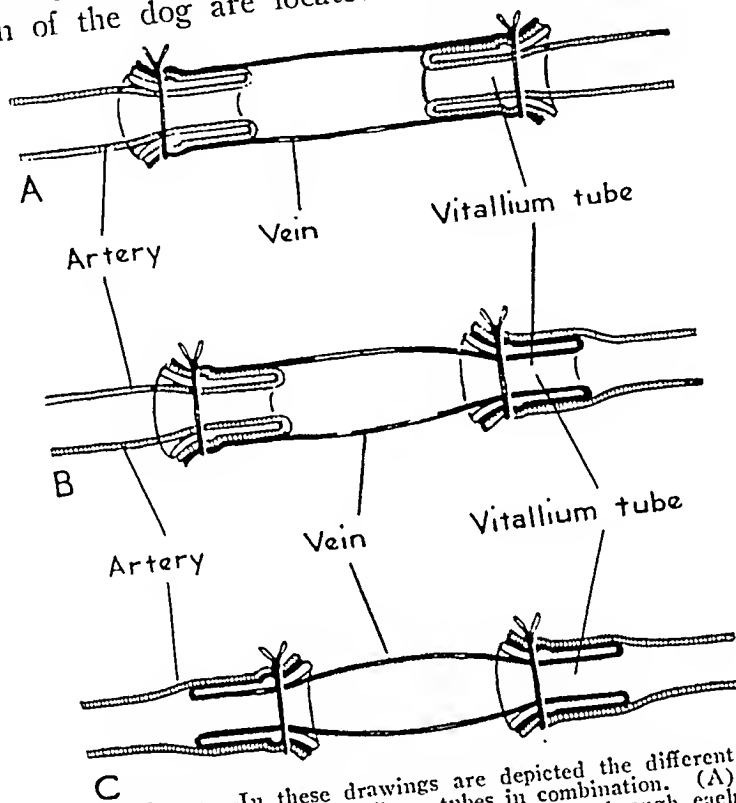


FIG. 2.—In these drawings are depicted the different methods of using two vitallium tubes in combination. (A) The divided ends of the artery are brought through each vitallium tube and everted; a ligature holds the everted artery in place; a vein transplant is then brought over each vitallium tube and held with ligatures. (B) The divided ends of the artery are brought through each vitallium tube and the everted vein is brought through each vitallium tube and the everted ends held in place by ligatures. The ends of the divided artery are brought over the vitallium tube and held in place by ligatures; this method makes it possible to bridge a gap of any length, the limiting factor being the length of the vein transplant. (C) A combination of the methods shown in (A) and (C).

8 cm., each branch being ligated close to the vein with arterial silk and loosely to the artery with fine silk. The segment of vein, 7 cm. long, is then excised between suture ligatures and promptly irrigated with saline solution through a blunt-nosed eye dropper. The distal end of the vein is identified so that it will be brought into approximation with the proximal end of the femoral artery, allowing blood to flow through the graft in the direction of the valves. One end of the vein is then pushed through the inside of the vitallium tube and the ends of the vein are everted over the tube for 1 cm. at each end. A single tie of fine silk near each end holds the vein in place. The tie is placed some 8 to 9 Mm. from the end of the tube. Care is taken from this point to allow nothing to touch the exposed intima of the vein and it is frequently moistened with saline solution. The femoral artery is then

divided after rubber-shod clamps have been applied. The ends of the artery are irrigated with saline solution and, with three mosquito clamps, each end of the artery is brought over the vitallium tube lined with vein for the distance of 1 cm. The ends of the artery are fastened to the tube beyond the ridges with two ties of fine silk at each end (Fig. 1 C). This maneuver

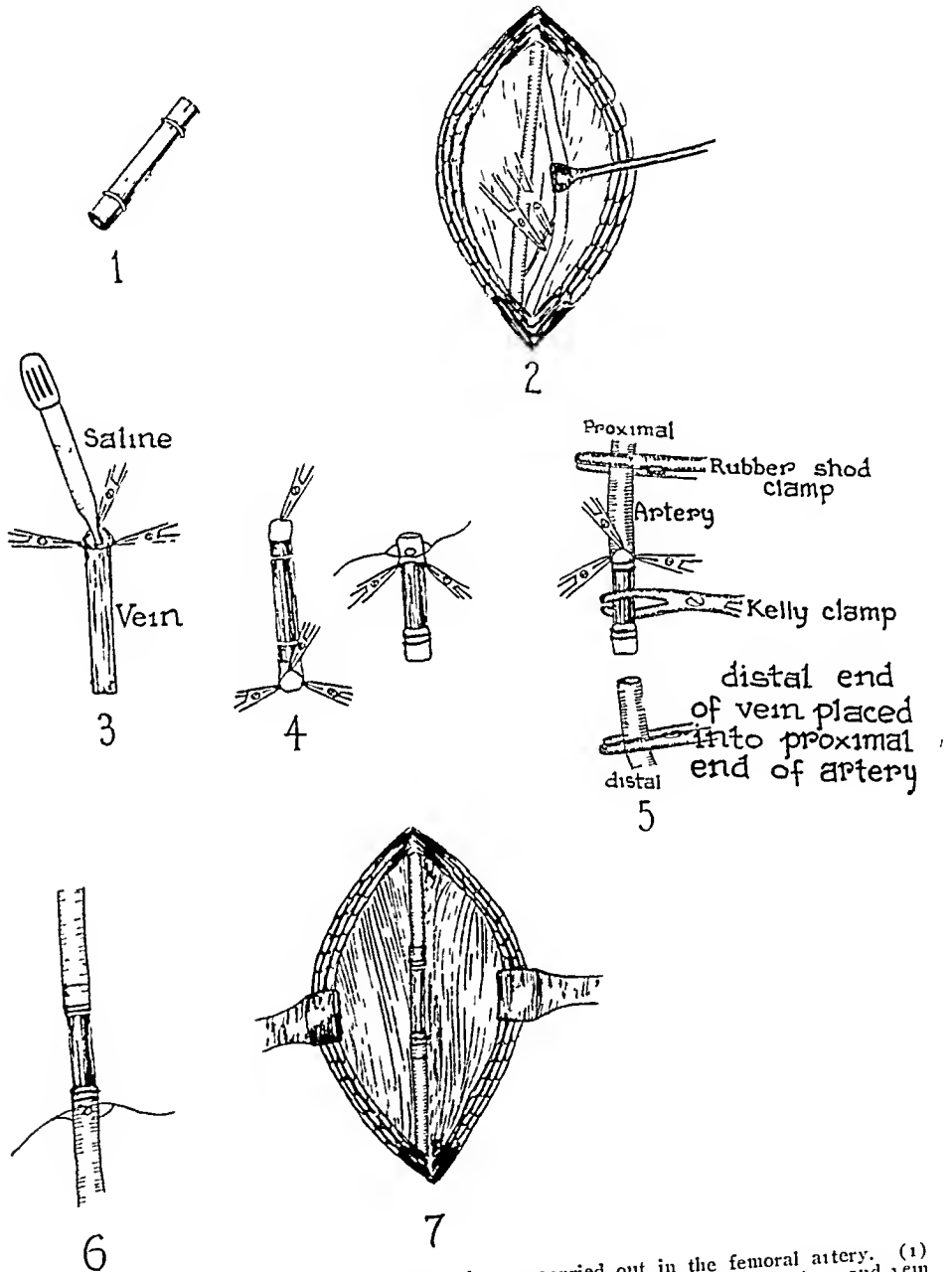


FIG. 3.—The various steps in the operation as carried out in the femoral artery. (1) The vitallium tube with its two ridges (sometimes grooves). (2) Shows the artery and vein exposed; the vein is retracted and clamps have been placed upon a branch. We now think it is perhaps better technic to ligate the branch first, clamp distally, and cut between. (3) The segment of vein upon removal is irrigated with saline solution through a blunt-nosed eye dropper. (4) The vein has been pushed through the inside of the vitallium tube; the two ends are everted over the ends of the tube and are held in place with one or two ligatures of fine silk. (5) The distal end of the segment of vein is placed into the proximal end of the artery and held there by two ligatures of fine silk; all ligatures are placed behind the ridges. (6) The snug ligature near the end of the vitallium tube, for the apposition of the artery and vein, is being tied. (7) The completed operation showing the femoral artery—a gap of two centimeters has been bridged.

results in the intima of the artery being in contact with the intima of the vein for 6 to 8 Mm. Finally, a tie of fine silk is tied loosely over the artery at each end, 1 to 2 Mm. from the end of the vitallium tube, so that blood cannot penetrate between the two intimas (Fig. 4) and, hence, form a thrombus in the first place; and, secondly, so that tissue juices released by the very tight ligatures cannot escape into the circulation. After the above has been completed the proximal rubber-shod clamp is released first in order that air bubbles will be driven peripherally. Immediately after release of the distal rubber-shod clamp the blood courses freely and a strong pulsation can be felt distal to the vitallium tube.

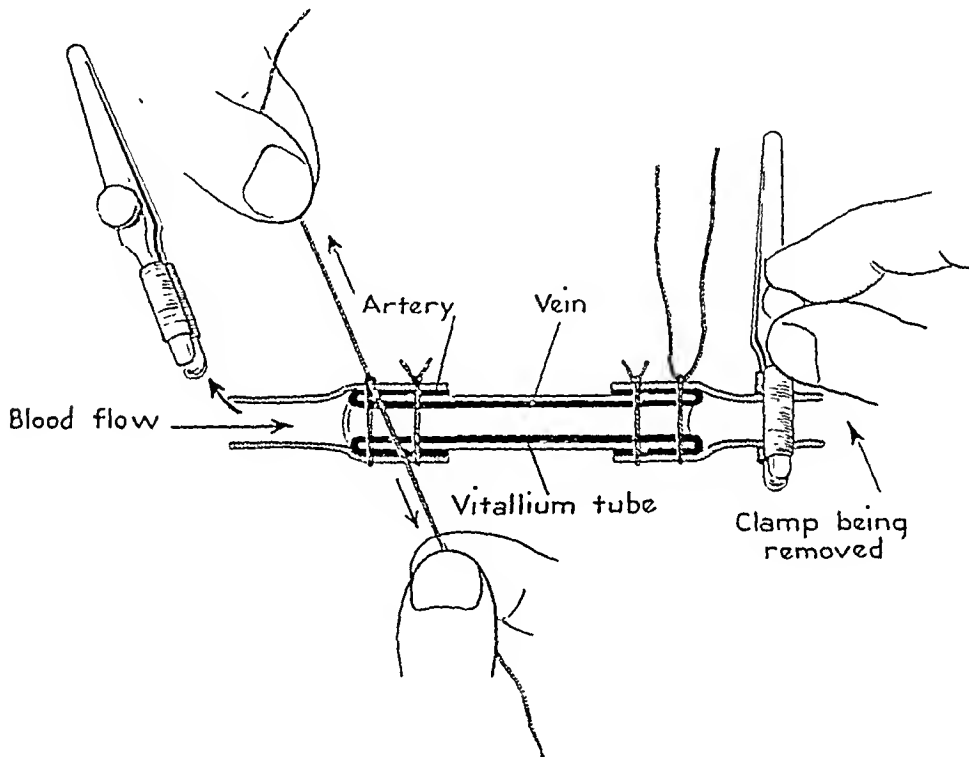


FIG. 4.—Illustrating the tying of the snug ligature near the end of the vitallium tube. This ligature prevents blood from penetrating between the two intimas and also keeps any tissue juice, freed by the crushing ligature, from escaping into the general circulation.

A modification of the above procedure has been made for the use of longer gaps in an artery. Two vitallium tubes with funnel ends are handled in a similar fashion to the above method (Fig. 2 C).*

We have used the nonsuture method in the anastomosis of the dog's abdominal aorta with regular success, grafts from the external jugular vein being employed to bridge the defect. Several of these animals have been followed now in excess of seven months, and their anastomoses have continued to function perfectly.

Clinically, we have used the two-tube method to bridge a combined defect of the popliteal and femoral arteries in a 63-year-old negro following

* For a more detailed description of the method refer to *Surgery*, 12, No. 3, 488-508. September, 1942.

excision of a syphilitic aneurysm. In spite of the presence of marked degenerative arteriosclerosis, gangrene of the leg was avoided.

Irrespective of the above encouraging results, it is our opinion that the acid test of the method is the study of its efficiency when used in anastomosing the small femoral arteries of dogs in clean and contaminated wounds, and without the use of anticoagulants.

The femoral artery of the dog was selected as a vessel for testing the efficiency of our nonsuture method of anastomosing vessels for the following reasons: (1) Abundance of experience has shown that suture anastomoses of the femoral arteries of dogs, with or without the use of vein grafts, fails



FIG. 5.—(A) Diodrast injection of the abdominal aorta in animal No. 1862 shows the right femoral artery to be entirely patent; the left side, however, is blocked some eight to nine centimeters above. This roentgenogram was taken 69 days postoperatively.

as often as it succeeds even when undertaken by skilled operators under rigid aseptic precautions, whereas the same technic may be employed to anastomose the aorta or carotid arteries with fairly regular success. (2) A review of the literature on the subject of methods employing a nonsuture prosthesis for the anastomosis of blood vessels reveals not a single instance of success in bridging defects of the femoral artery in dogs using vein grafts.

In Figure 5 is shown an arteriogram of a dog's femoral vessels 69 days after anastomosis of each femoral artery using the single tube method. The anastomosis of the right femoral artery is evidently patent, whereas thrombosis has taken place on the left, although this anastomosis had been proven

to be patent on exploration 33 days after anastomosis had been performed. Figure 6 is a photograph illustrating a probe through the excised anastomosis of the right femoral artery. The sheath of the femoral artery has healed about the tube without evidence of irritation by the vitallium, and the tube can be seen shining through the thin sheath of the artery.

Figure 7 is a photograph of a specimen of an anastomosis of the femoral artery excised 35 days after the insertion of a vein graft over a single vitallium tube. The latter has been removed and one end of the anastomosis opened to expose the smooth healing of the intimas of the artery and vein. A photomicrograph of the previous specimen shows that the intima has bridged the artery-vein junction (Fig. 8). Firm healing has occurred between the artery and vein. The vein graft appears essentially normal and well nourished.

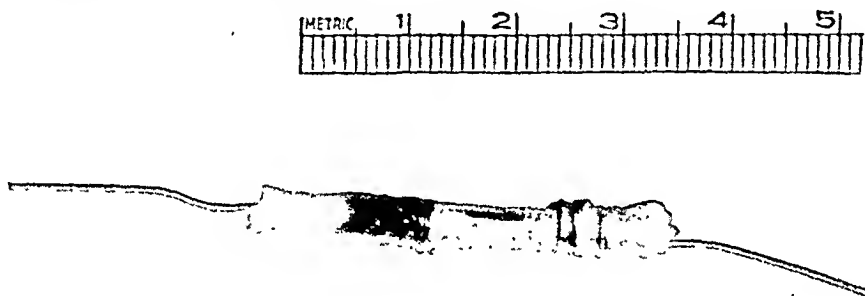


FIG. 6.—Specimen of the right femoral artery of animal No. 1862 showing minimal reaction around the vitallium tube, and the silk ties to have remained in place; complete healing has occurred between the intima of the vein and that of the artery at each end.

and this is important because of the fact that in the single tube method of anastomosis the vein graft is completely isolated from the perivascular tissues.

The use of a vein is the only practical means of successfully bridging a sizable arterial defect. Therefore, a method of anastomosing arteries to be of service in the war-wounded, and of maximum service clinically, must, of necessity, be easily adaptable to the use of vein grafts. Such is not the case with the suture method under war conditions. Increasing experience with nonsuture method, with strict attention to details of technic and asepsis, and the use of generous segments of femoral vein from the opposite leg, affords a 90 per cent expectancy of success in bridging defects in the small femoral arteries of dogs.

ANASTOMOSIS OF BLOOD VESSELS IN CONTAMINATED WOUNDS

Experience has shown that infection is the greatest single cause of failure in any method of blood vessel anastomosis. It has long been known that the wound may heal by primary union and yet cultures taken from the site of the anastomosis may reveal bacterial growth. Experiments were conducted in which the Carrel suture technic was employed to anastomose free vein transplants to the divided ends of the femoral arteries of dogs (Table I). The operation was performed six hours after unsterile ligation and division

TABLE I

RESULTS WITH CARREL SUTURE TECHNIC EMPLOYING FREE VEIN TRANSPLANT BETWEEN DIVIDED ENDS OF FEMORAL ARTERY OPERATION PERFORMED 6 HOURS AFTER UNSTERILE LIGATION AND DIVISION OF FEMORAL ARTERY			
Perfect Function and Structure (14 Days)	Perfect Function but Aneurysm (14 Days)	Thrombosed (14 Days)	Secondary Hemorrhage (3-7 Days)
1	3	2	4

of the femoral artery. One and one-half grams of sulfanilamide was used in alternate wounds in the series, and all of the wounds were thoroughly irrigated before performing the anastomoses. Of the ten anastomoses, one was found to be successful upon exploration 14 days postoperative, while aneurysm occurred at the site of the anastomosis in three instances, thrombosis occurred in two, and secondary hemorrhage in the remaining four. Figure 9 is a photograph of the specimens showing aneurysms at the site of the anastomoses. Cultures taken from the aneurysms revealed bacterial growth, as was the case in the rest of the failures.

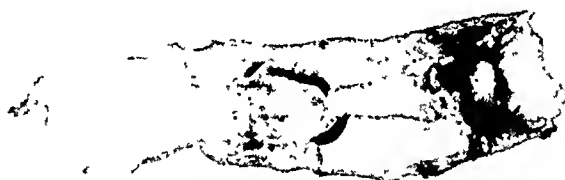
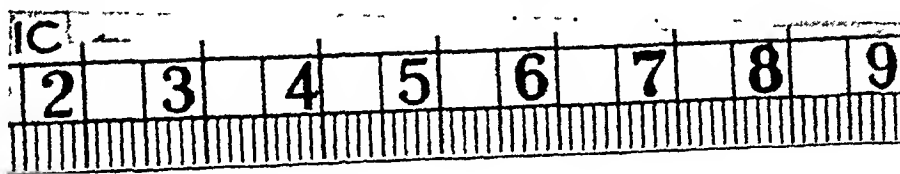


FIG. 7.—A photograph showing the opened specimen of the left femoral artery, where excellent healing has taken place between the intimas of the artery and vein. The vitallium tube has been removed and the vessel is entirely patent; this having been demonstrated by sectioning the artery distal to the anastomosis. It is interesting, however, that a diodrat injection made just before the animal was sacrificed failed to demonstrate patency.

Table II shows the results with the nonsuture method of bridging arterial defects in the femoral arteries of dogs using the double tube vein graft technic. The operation was performed six hours after unsterile ligation and

TABLE II

RESULTS WITH NONSUTURE METHOD OF BRIDGING ARTERIAL DEFECT IN FEMORAL ARTERY OPERATION PERFORMED 6 HOURS AFTER UNSTERILE LIGATION AND DIVISION OF FEMORAL ARTERY			
Perfect Function and Structure (7 Days)	Perfect Function but Aneurysm (7 Days)	Thrombosed (7 Days)	Secondary Hemorrhage (7 Days)
12	0	10	0

division of the artery, and, again, 1.5 Gm. of sulfanilamide was used in the wounds of alternate dogs. Of the 22 anastomoses performed, 12 were successful, and thrombosis occurred in 10.*

* The anastomoses were explored on the 7th postoperative day because experience has shown that if the anastomoses remain patent up to the 7th day, thrombosis is extremely unlikely to occur thereafter, whereas with suture anastomoses failure is likely to occur up to 14 days after operation.

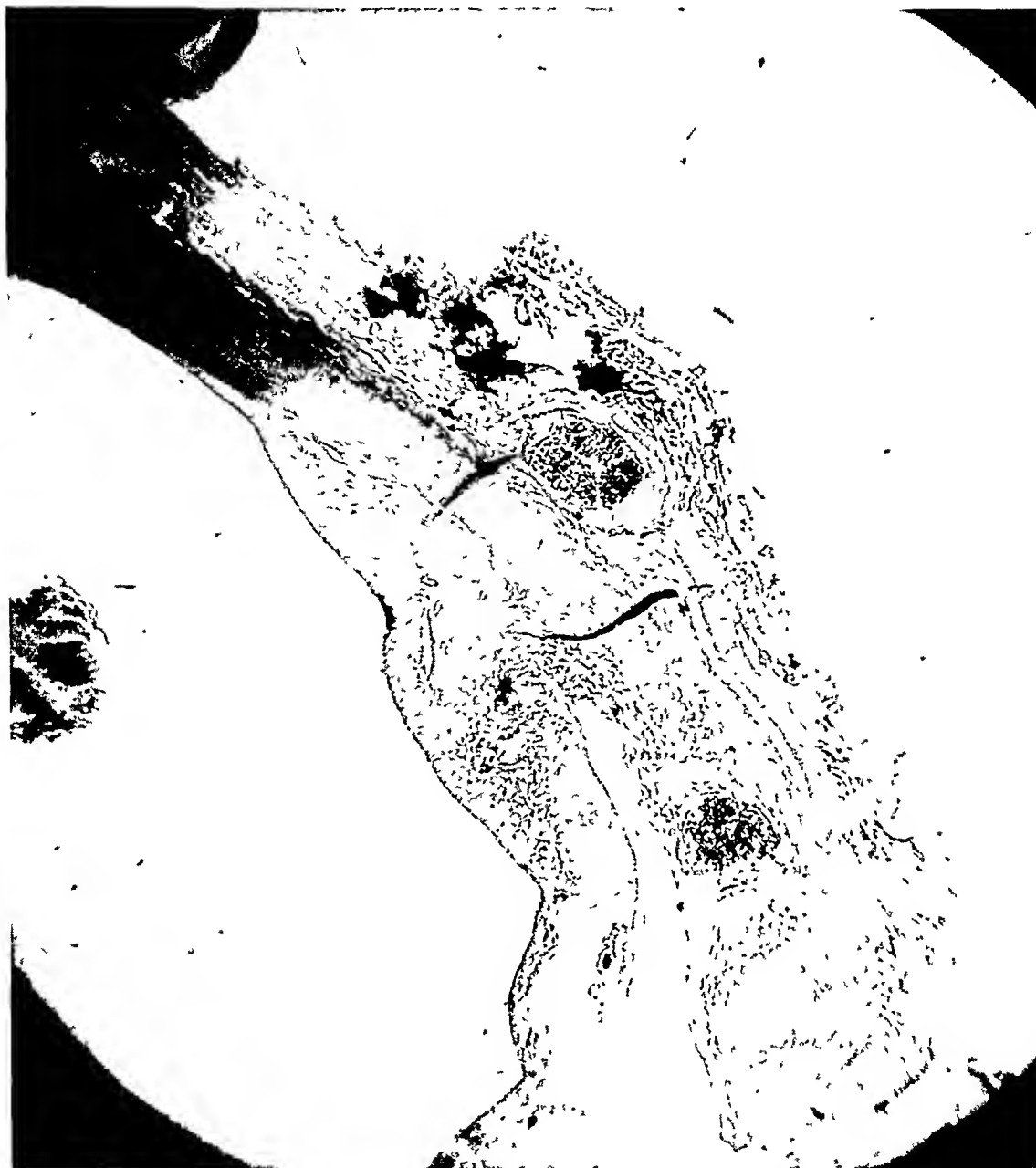


FIG. 8.—Photomicrograph of specimen removed from animal No. 1880 showing the junction of the artery and vein. This junction has been bridged by intima.

A comparison of these two series of animals reveals the dire results of suture anastomoses of arteries in the presence of bacterial contamination. It is of interest to note that sulfanilamide was used in the one successful experiment, whereas with the nonsuture method, using vitallium tubes, the anastomoses succeeded in over 50 per cent of the experiments in spite of bacterial contamination. In the failures, unlike the suture method, simple thrombosis occurred without secondary hemorrhage.

Table III: In this series of ten animals the following changes were made:

1. The performance of the anastomosis was delayed 24 hours after unsterile ligation and division of the femoral artery.
2. The dirty wounds were débrided before performing the nonsuture anastomoses.

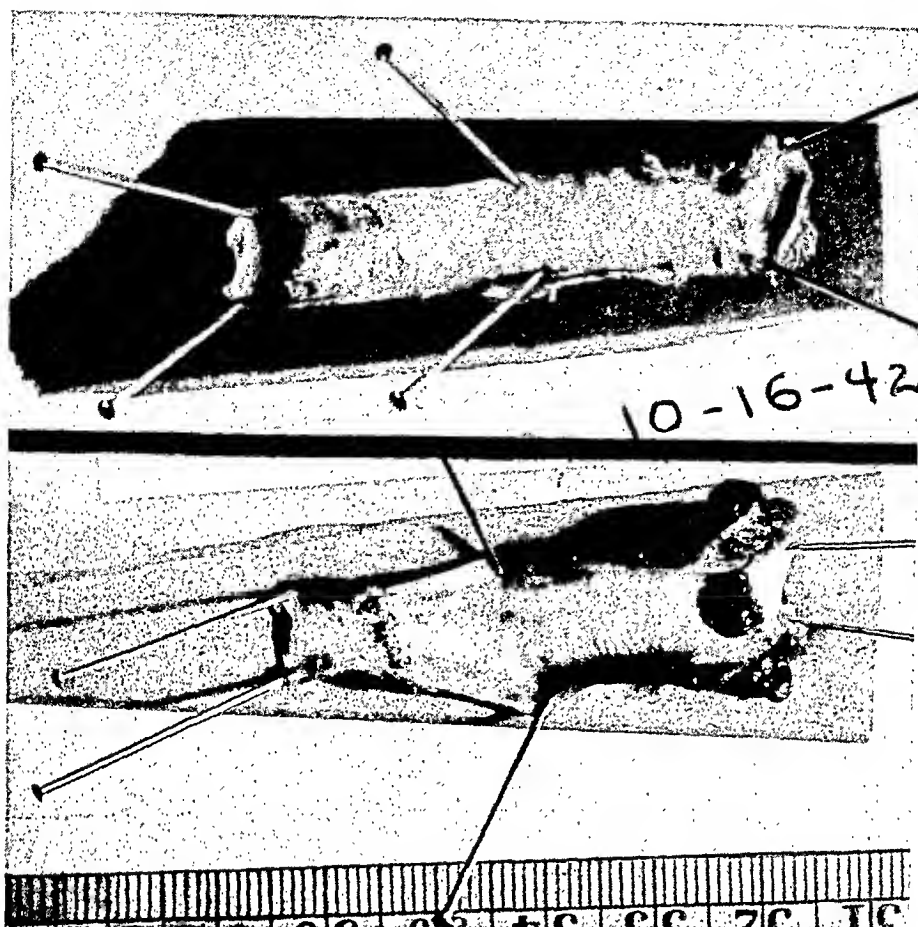


FIG. 9.—Specimens showing aneurysms at the sites of anastomoses; note the aneurysms in the upper right of animal No. 1987 and the lower right of animal No. 2018. This latter one is almost completely filled with thrombus.

3. Sulfanilamide was placed in the wounds of alternate dogs.
4. The vein graft was taken from the opposite leg, and in generous lengths, to avoid tension upon the anastomosis.

Results: Success in three of ten anastomoses.

TABLE III

RESULTS WITH NONSUTURE METHOD OF BRIDGING ARTERIAL DEFECT IN FEMORAL ARTERY
OPERATION PERFORMED 24 HOURS AFTER UNSTERILE LIGATION AND DIVISION OF FEMORAL ARTERY
NO SULFATHIAZOLE

Perfect Function and Structure (7 Days)	Perfect Function but Aneurysm or Partial Thrombosis (7 Days)	Thrombosed (7 Days)	Secondary Hemorrhage (6 Days)
3	1	5	1

The successes in this group of 24-hour delayed anastomoses three out of ten represents a reduction of 25 per cent when compared with 12 out of 22 successes in the six-hour delayed anastomosis group of Table II. This "fall off" in success occurred in spite of the fact that in the 24-hour group the wounds were carefully débrided immediately before performing the anastomoses.

Whereas the gross appearance of the wounds of the two series differed little during healing, the behavior of the anastomoses in the two groups

reflected, with remarkable sensitiveness, the true bacteriologic status of the two groups of wounds, namely, the state of bacterial contamination in the six-hour group and spreading infection in the 24-hour group. It is fair to state, however, that sulfanilamide was placed in the wounds at the time of the performance of the anastomoses in two out of the three successes in the 24-hour group.



FIG. 10.—Photograph of two dogs, No. 2110 (12 days) and No. 2092 (21 days) postoperatively; in which the right hind leg was amputated at the midhigh level and reimplanted after having been kept in cracked ice for 24 hours. Moderate edema is still present in the 12-day animal.

Table IV: The experiments in this series of ten dogs are identical with the former series (Table III) except that each dog received one gram of sulfathiazole by mouth twice daily from the time of the initial unsterile wound until the day of examination of the anastomosis one week later. Results: Success in eight out of the ten anastomoses, and one of the two failures was thought to be due to a technical difficulty in dealing with a venous valve.

TABLE IV			
RESULTS WITH NONSUTURE METHOD OF BRIDGING ARTERIAL DEFECT IN FEMORAL ARTERY			
OPERATION PERFORMED 24 HOURS AFTER UNSTERILE LIGATION AND DIVISION OF FEMORAL ARTERY			
Perfect Function and Structure (7 Days)	Perfect Function but Aneurysm (7 Days)	Thrombosed (7 Days)	Secondary Hemorrhage (7 Days)
8	0	2*	0

Table V is identical with the former series (Table IV) except that Carrel suture anastomoses were performed in the ten animals. Results:

* One of these two was transporting blood satisfactorily but after removal examination revealed partial thrombosis to have occurred within the vein near the proximal tube.

Four out of ten anastomoses were completely successful. Thrombi were found at the site of the anastomoses in four cases, complete thrombosis in one, and secondary hemorrhage in one case.

TABLE V

RESULTS WITH CARREL SUTURE TECHNIC EMPLOYING FREE VEIN TRANSPLANT
BETWEEN DIVIDED ENDS OF FEMORAL ARTERY
OPERATION PERFORMED 24 HOURS AFTER UNSTERILE LIGATION AND DIVISION OF FEMORAL ARTERY

Perfect Function and Structure (14 Days)	Perfect Function but Aneurysm or Partial Thrombosis (14 Days)	Thrombosed (14 Days)	Secondary Hemorrhage (4 Days)
4	4	1	1

In addition to the simplicity and rapidity of the performance of the non-suture technic in comparison with that with the Carrel suture, the former succeeds far more regularly in the presence of bacterial contamination. The high percentage of favorable results (80 per cent) obtained with our non-suture method in anastomosing the small femoral arteries of dogs in 24-hour-old, dirty wounds, encourages us to believe that the method will succeed, when used in conjunction with the sulfonamides, if employed for the anastomosis of severed arteries in the war-wounded. It is our experience, and but logical to conclude, that the use of the method upon larger vessels will contribute to its greater success. It is reasonable to believe that in the clinical application of the method the factors of rest, wound splinting and postoperative care; the elimination of pain and vasospasm; and the possible use of anticoagulants would insure its success.

BASIC REQUIREMENTS OF A METHOD OF ANASTOMOSING BLOOD VESSELS IN THE WAR-WOUNDED

I. The method must afford a high incidence of success when used in badly contaminated wounds up to 24, or more, hours after injury.

II. The method must be adaptable to the use of vein grafts for bridging arterial defects without complicating the technic or efficiency of the method.

III. The method must be simple.

Our experiments with the nonsuture method, when used in conjunction with the sulfonamides, affords convincing evidence that the method will fulfill requirement I. The method, employing the double tube technic, is peculiarly adaptable to the use of vein grafts, thereby fulfilling requirement II, whereas, the use of variable-sized vein grafts complicates the technic and greatly extends the performance time of suture anastomoses. As to requirement III, the very simplicity of the nonsuture method commends its use in surroundings as crude and bare of equipment as the necessity of war may dictate.

It is our sincere opinion that the nonsuture method of anastomosing vessels, as presented, meets all the requirements for successful anastomosis of the severed primary arteries in the war-wounded. The one factor affecting the benefits from the method in this war would be the extent to which it is used. Throughout the history of wars there is no greater dilemma than that

faced by the surgeon in regard to the rationing of treatment to the wounded under the pressure of battle. In the last world war, for example, to what purpose would be the contemplation of a method of anastomosing a severed artery when, on a given occasion, there may be several soldiers whose lives needed saving.

In consideration of a method of saving limbs in this war first thought must then be given to the question to what extent will surgical care be rationed? At the onset of the present European war, because of rapidly shifting battle fronts due to mechanized warfare, it became obvious that the seriously wounded would have to be operated upon and cared for in base hospitals far removed from the front, and the ambulance plane became the solution to the problem of evacuation of the seriously wounded. Once the plane is in the air it does not necessarily have to land its wounded at any one overworked base hospital. The wounded may be flown to hospitals where, under favorable conditions, experienced surgical teams can operate, and where postoperative care can be carried out continuously by the same team. The constantly shifting battle line requires the use of numerous mobile first aid and evacuation units where hemorrhage may be controlled, shock treated, bone splinted, and chemotherapy administered before evacuation of the seriously wounded. The above system has already successfully met the challenge in practice upon the Russian and other battle fronts in this war. It has proven sufficiently swift for the successful treatment of serious cranial, chest and gunshot wounds of the abdomen. It is our opinion that the clinical course of the average case of severe extremity wound with severed primary artery lends itself to successful handling in this manner. The following is a case in point:

Case Report.—A 40-year-old junk dealer was admitted to Presbyterian Hospital in deep shock. Three hours before, the patient had fallen beneath the wheels of his loaded wagon and the wheels had passed over the back of his right leg, causing a crushing laceration of all tissues superficial to the bone just above the knee joint. Following a transfusion of 1000 cc. his blood pressure rose and the wound began to bleed again. The leg which was cold and pulseless began to warm slightly and assume a slightly pink color. Exploration of the hematoma, which had dissected most of the posterior muscle planes of the thigh to below the knee, revealed the retracted ends of the popliteal artery which had been crushed against the femur. Blood clot was thoroughly evacuated. The ends of the artery were ligated with silk. The popliteal vein had been crushed and had become thrombosed. It was ligated above the thrombus with silk. The wound was thoroughly débrided, irrigated with saline, and sulfanilamide was implanted into the wound, which was left open and the leg splinted. Sulfadiazine was given intravenously and continued by mouth.

Subsequent to operation the leg was placed at heart level. The location of the wound precluded the use of the Pavaex boot. The blood pressure was maintained and anemia corrected postoperatively by transfusions, and an alcohol block of the lumbar sympathetic nerves on the right was carried out. The man's pain was controlled by opiates. Under continued sulfonamide therapy, the clinical course of this man from this point on was of extreme interest. In the first place, throughout his entire postoperative course the patient developed no evidence of infection either in the wound or systemically. For the

first 36 hours there was no disagreement on the question of sufficient circulation to the foot to maintain life. The veins emptied freely on slight elevation and filled slowly at heart level. The foot was fairly warm and of pale but living color. After an interval of 48 hours traumatic edema began to register its first deleterious effect upon the circulation, as evidenced by slight obstruction to venous return. These effects became increasingly manifest as venous engorgement, cyanosis and slight edema of the foot and ankle through the 3rd and 4th days after injury developed. But it was not until the 4th and 5th days that a declining temperature of the foot heralded the beginning of strangulation of the arterial collateral flow. From then on the tissue damage from anoxia became rapidly irreversible and gangrene was full blown by the 7th day after injury.

We have presented the above case in some detail because it illustrates well some important clinical facts. In the first place the case is not dissimilar to a war wound. In illustrating the benefits of sulfonamide therapy, the conclusion seems inescapable that the onset of gangrene in this case was greatly postponed by the control of infection. One, likewise, gathers the impression that had there been a little more collateral circulation present, the period of traumatic edema might have been successfully tided over. It was equally obvious that a successful anastomosis of the popliteal artery performed at any time up to the 5th day after this man's injury would have saved his leg. Even after the onset of edema, reestablishment of blood flow through the artery would have permitted elevation of the leg with subsidence of the edema.

It is our opinion that a war wound case of the above type may be successfully handled as follows:

Control of hemorrhage (preferably ligation of the bleeding vessels).

Treatment for shock and administration of chemotherapy by the first aid and evacuation units.

Transfer by ambulance plane to a base hospital for débridement and evaluation of the status of the collateral circulation.

Anastomosis of the primary artery may be undertaken when and if indicated.

Our experience with the nonsuture vein graft method, when used in conjunction with the sulfonamides in anastomosing arteries in infected wounds 24 hours after unsterile ligation, indicates a likelihood of functional success.

HETEROPLASTIC VEIN GRAFTS

By heteroplastic we mean a vein graft transplanted from one subject to another. In contemplating the use of the nonsuture method of anastomosing vessels under circumstances more adverse than the facilities afforded by a base hospital, we concede advantages attending the use of heteroplastic grafts. For example, the time necessary for completion of an anastomosis by an average operator with a vein graft at hand does not exceed 15 minutes. Important questions arise in considering the use of heteroplastic vein grafts for bridging arterial defects in the war-wounded. (1) How long would it

be necessary for an anastomosis to function to prevent the occurrence of gangrene? There is clinical and experimental evidence to support the opinion that if an anastomosis functions beyond the period of posttraumatic edema, up to 14 days, the limb will be saved. Reichert⁷ amputated (cutting all tissues except bone, large nerves, femoral artery and vein) and replanted the hind legs of dogs and showed that arteries developed across the replant line on the 3rd postoperative day. Veins and lymphatics regenerated on the 4th and 5th days. He, likewise, proved that the regenerated vessels were functionally adequate on the 8th postoperative day by ligation of the femoral artery and vein without the occurrence of gangrene. However, if the artery itself is ligated alone gangrene of the leg can not be prevented until after the 14th day.

(2) Will heteroplastic vein grafts function adequately when used to bridge vessel defects? To gain information on this important question we performed the following experiments. Figure 10 is a photograph of two dogs in which the right hind leg was amputated at the midhigh level. After an interval of 24 hours the legs were reimplanted, using the nonsuture two-tube technic and vein grafts from a 3rd and 4th animal to bridge the defects in the femoral artery and vein. The amputated limbs were preserved during the 24-hour interval in cracked ice. The dogs were given sulfathiazole, one gram twice daily, by mouth, from the time of the first operation. The photographs were made 12 and 21 days, respectively, after reimplantation of the limbs, and there is every evidence of a good supply of arterial blood in these reimplanted legs. Correlation of these experiments with the informative studies of Brooks and Duncan¹¹ on the effects of temperature on the survival of anemic tissue is of interest.

The survival of the legs in these two dogs depended solely upon the function of vein segments transplanted from other dogs, and in this sense the experiments are critical. However, we have used heteroplastic vein grafts to bridge femoral artery defects in seven additional dogs. The anastomoses functioned for 17 days (average), which is well beyond the postulated 14 days of posttraumatic edema.

The present surgical trend of removing the great saphenous vein in ligating incompetent communicating veins has afforded us an opportunity of examining a number of these veins. We found that the average great saphenous vein is suitable for use as a vein graft for bridging arterial defects using our nonsuture method. The vein may be removed in lengths up to 40 cm., and is adaptable for use with vitallium tubes varying in diameter from 4-7 Mm. This means that the average great saphenous vein would be technically and functionally adequate for bridging defects in arteries varying in diameter from 4-12 Mm. This range of diameters would include the carotid artery or any artery one should care to anastomose in the extremities. The performance of our nonsuture method of anastomosis is not complicated by wide differences in diameter between the vein segment and the ends of the artery to be anastomosed. From a functional point of view, differences

in diameter up to 50 per cent are of relative little concern, for Mann⁸ has shown that the lumen of an artery may be narrowed 50 per cent without affecting the volume of blood flow through the vessel. It is not until the lumen has been constricted in excess of 75 per cent that a sharp decline in volume flow occurs. What does occur, of course, at the site of a somewhat narrowed anastomosis, is a compensating increase in the rate of blood flow and this, in itself, is a protection against thrombosis at the site.

PRESERVED VEIN GRAFTS

We are now conducting experiments to determine the length of time that segments of veins may be preserved and function successfully when used to bridge arterial defects in dogs. Carrel⁹ showed that segments of artery preserved up to five weeks in a refrigerator functioned indefinitely when used as heteroplastic grafts to bridge arterial defects in dogs. It is fortunate that in this war the equipment for preserving the segments of veins, the refrigerator, will be always fairly close at hand.

The most practical source of supply for veins suitable for use in bridging arterial defects in the war-wounded in active battle areas is *via* the pathologist. Segments of great saphenous, femoral, jugular or almost any sized veins may be removed aseptically by the pathologist. These veins may be placed in sterile test tubes and preserved in refrigerators against an occasion for emergency use. In less active battle areas, with the system of refrigeration it has been necessary to maintain for the transportation of blood plasma, it is not inconceivable to work out a plan for supplying great saphenous veins from civilian hospitals.

The one important thing to remember is that with a vein at hand, a severed carotid, or an artery in an extremity, may be quickly joined together by using the simple nonsuture method of blood vessel anastomosis.

SUMMARY

The problem of blood vessel anastomosis deserves important consideration in this war because (1) advances in the control of serious infection and the possible use of anticoagulants afford, for the first time in the history of wars, a basis for success; (2) the outstanding cause of the loss of limbs in this war will be damage to the blood supply.

We present vitallium as a nonirritating alloy suitable as a prosthesis for a vein graft bridging an artery or vein defect in a nonsuture method of vessel anastomosis using a single or double tube technic.

We have presented carefully controlled experiments on dogs demonstrating that sulfathiazole by mouth contributes greatly to the success of delayed anastomoses of severed vessels in contaminated wounds. Using sulfanilamide in alternate wounds in a series of 77 anastomoses we have noted it to be of moderate but definite value.¹⁰

The nonsuture method was shown to be highly successful in anastomosing

the small femoral arteries of dogs, even in contaminated wounds 24 hours after section of the artery, and without the use of anticoagulants.

We postulated that vein graft anastomoses of the severed primary artery in the war-wounded would prevent the loss of the extremity by gangrene if the anastomosis remained patent beyond the period of posttraumatic edema, up to 14 days.

Experiments are presented showing that veins taken from one dog may continue to function in another when used as transplants to bridge vessel defects. For example, the successful reimplantation of limbs 24 hours after their removal. These experiments afford a prospect for the use of preserved veins as grafts for bridging vessel defects in the war-wounded as an alternate to the use of homoplastic transplants.

CONCLUSIONS

If, as stated in the British War Memorandum, the indications for amputation are to be based primarily upon the integrity of the main blood vessels, a simple, quick method of joining vessels together should have much to commend it in this war. The control of serious infection, and the possible use of anticoagulants, would seem to insure success of the method.

BIBLIOGRAPHY

- ¹ Medical Department of the U. S. Army in the World War. Surgery, 11, Part I, 719. Government Printing Office, Washington, 1927.
- ² Medical Department of the U. S. Army in the World War. Medical and Casualty Statistics, 15, Part II, 1017. Government Printing Office, Washington, 1925.
- ³ Makins, G. H.: Gunshot Injuries to the Blood Vessels. John Wright and Sons, Ltd., London, Eng., 1919.
- ⁴ Matas, R.: Keen's Surgery, Supplementary Vol., 7, Chapt. 24. 737-819, W. J. Saunders Co., Philadelphia, 1921.
- ⁵ Holman, E.: War Injuries to Arteries and Their Treatment. Surg., Gynec., and Obst., 75, 183, August, 1942.
- ⁶ Fairbank, H. H. T., Surg. Rear Admiral G. Gordon-Taylor, and Col. C. Max Page: Emergency Amputations. War Medicine, 2, 147-153, 1942.
- ⁷ Reichert, F. L.: The Importance of Circulatory Balance in the Survival of Replanted Limbs. Bull. Johns Hopkins Hospital, 49, 86, 1931.
- ⁸ Mann, F. C., Herrick, J. F., Essex, H. E., and Blades, E. J.: Effect on Blood Flow of Decreasing Lumen of Blood Vessels. Surgery, 4, 249-252, 1938.
- ⁹ Carrel, A.: Results of the Transplantation of Blood Vessels. Organs and Limbs. J. A. M. A., 51, 1662-1667, 1908.
- ¹⁰ Lord, J. W., Jr., Blakemore, A. H., and Stefko, P. L.: Unpublished data.
- ¹¹ Brooks, Barney, and Duncan, George W.: The Effects of Temperature on the Survival of Anemic Tissue: An Experimental Study. ANNALS OF SURGERY, 112, 130-137, July, 1940.

THE INTRACTABLE DUODENAL ULCER*

EVALUATION OF SURGICAL PROCEDURES

J. WILLIAM HINTON, M.D.

NEW YORK, N. Y.

DURING THE PAST DECADE even surgeons have admitted that medical management is the treatment of choice for duodenal ulcers and that surgical intervention should be confined to the intractable cases. The decision as to intractability varies greatly in different hospitals and clinics and the indications for operation which were used a generation ago are frequently used today, namely, obstruction, massive hemorrhage, a perforating ulcer, and the fact that the patient refuses to cooperate under medical management. It is perhaps because of the elasticity of indications for surgical intervention that gastro-enterologists question the advisability of any type of surgical procedure for duodenal ulcer.

My impressions, based upon 15 years experience in stomach clinics, lead me to question the above named indications for surgical intervention. On the Fourth Surgical Division of Bellevue Hospital we have observed 1,328 ulcers, representing 25,218 visits, and at Post-Graduate Hospital, since 1931, 676 ulcers have been seen, representing 7,628 visits. During the past ten years, in our experience, the only true indication of intractability in the case of a duodenal ulcer, has been constant pain. Relief from the continuous pain can not be obtained under any form of medical management, and sedation is frequently necessary to induce sleep.

Pyloric obstruction is still referred to in the literature as a true indication for surgical intervention. The stenosing and obstructing ulcer has recently been reviewed by Allen,¹ who states that the stenosing lesion "finally becomes a mechanical problem and the patient seeks help because he can no longer absorb nourishment to maintain life. The onset of such a condition is a gradual one, and the end-stage is reached so insidiously that one often finds that the stomach has become enormously dilated. It is interesting that such an organ emptying infinitesimal amounts of its contents into the duodenum, can exist within a person and create so little distress." In the two clinics with which I am associated, it has been our experience that a stenosing or obstructing ulcer, not accompanied by pain, does not require surgical intervention. These patients can be relieved by medical management and obstruction does not recur provided they remain free from pain.

Wilkinson² emphasizes the duration of the obstruction as the important factor. He states that an obstruction of three months duration, or less, will respond satisfactorily to medical management but in the case of an obstruction of three months, or longer, recurrences are almost certain and

* Read before the Surgical Section of the New York Academy of Medicine, December 4, 1942.

INTRAC TABLE DUODENAL ULCER

operation is usually indicated. He does not mention pain as a factor in causing the obstruction. In our experience, obstruction without pain is due to edema and pyloric spasm and not to scar tissue around the pylorus. Since 1932 no patient with so-called pyloric obstruction accompanied by severe pain, has been referred for surgical intervention, either in private consultation or in the clinics.

The exceptions to the above statement occurred in 1930 and 1931, when simple closure was done for perforated duodenal ulcers. Nine months after



FIG. 1.—Penetrating posterior duodenal ulcer with symptoms of two months' duration. Operation advised by internist and roentgenologist.

operation in the case of one patient, and two years afterwards in the case of another, a true organic obstruction developed from the operative procedure, necessitating a short-circuiting operation. Neither of these patients was suffering from pain.

Massive hemorrhage, occurring once or oftener, as an indication for surgery brings up a controversial question. First of all, we do not have a clear-cut line between what constitutes massive and moderate hemorrhage, and a study of the literature reveals the elasticity in the grouping of these cases. However, if we all agree that a red blood cell count of 2,000,000 or less, a hemoglobin if less than 40 per cent, and lowered blood pressure with

a moderate degree of shock, constitutes massive hemorrhage, then we are obviously agreed that the patient has suffered a great loss of blood.

Surgical management of these patients may be considered under two headings: Surgical intervention in the stage of acute hemorrhage, which is occasionally indicated; and second, surgery as an elective procedure to prevent further hemorrhage. My views regarding the first mentioned type of management have been expressed in previous publications.^{3, 4} The indications for surgery as an elective procedure are interpreted differently in different hospitals. The point emphasized by Allen⁵ as to the dangers of massive hemorrhage in the different age-groups has been fairly universally accepted. That is, in a patient over 45 years of age, the prognosis is serious, while in a patient under 45, massive hemorrhage rarely proves fatal. Blackford and Cole⁶ have confirmed this observation. Blackford and Allen,⁷ in a report of 151 fatal hemorrhages, record that in only 35 cases, or 23 per cent, was there a history of previous hemorrhage, or in other words, 77 per cent of the fatalities occurred following the first hemorrhage—an interesting observation, with definite clinical significance. These authors also observed that 34, or 23 per cent of the deaths occurred at home. We have always felt, in considering massive hemorrhage from peptic ulcer, that unless patients are admitted under similar conditions the severity of the hemorrhage may be different. In a hospital with an active ambulance service the type of cases is different from those in the average hospital. The report of Blackford and Allen⁷ indicates that, not infrequently, patients die at home before ever reaching a hospital. They state that fatalities in patients under 45 are rare, whether or not patients receive treatment, and that in patients under 40 fatalities are almost unknown. On this point, we must disagree. Since 1937, on the Fourth Division at Bellevue Hospital, I have had occasion to operate upon three patients who were medical failures, having had chronic ulcers for periods averaging from 5 to 15 years. These patients were suffering from intractable pain and were being prepared for operation on the surgical wards, when they had massive hemorrhages. Amazingly enough, all of them occurred within 24 to 48 hours of the day set for the elective operation. This group of cases included two duodenal ulcers perforating into the pancreas, and one gastrojejunal ulcer eroding into the transverse mesocolon and the pancreas. All three patients were saved by operative intervention. Massive blood transfusions were given before, during and after operation, and a subtotal resection was performed in each case. The patients were 27, 37, and 42 years old, respectively. Two patients were admitted as emergencies, with whom we had had no previous contact. One of them, 44 years of age, had a duodenal ulcer and the other, 33 years old, had a gastric ulcer. A subtotal resection was performed in each instance. The former patient died, the latter lived. There has been one other case in our division, a gastric lesion that resulted in a fatality while the author was out of town, but this case was proved at autopsy to be not an ulcer but a small ulcerating carcinoma.

INTRACTABLE DUODENAL ULCER

From 1928 to 1937 we encountered an average of 13 massive hemorrhages a year, according to the definition of massive hemorrhage as previously described, and there was a medical mortality of ten per cent, while during the past six years, 1937 to 1942, inclusive, with surgical intervention in the desperate cases which do not respond to continuous transfusions, we have lost but one case from massive hemorrhage after surgical intervention, and none under medical management.

The penetrating or perforating duodenal ulcer, as diagnosed roentgenologically, does not necessarily constitute a true indication for surgical inter-



Fig. 2.—After three weeks' observation on the surgical wards.

vention. Here, again, one must rely on the clinical evaluation of the symptomatology. If the patient has had an ulcer for years, with intractable pain, then the indications are obvious, but if he has had an ulcer for only a short period of time, which proves to be a penetrating ulcer, medical management will very frequently relieve the symptoms and the niche will disappear.

The following case was referred to me for operation in January, 1941. The patient was a young man, 24 years of age, with a history of ulcer of two months duration. Roentgenograms revealed a penetrating posterior duodenal ulcer (Fig. 1), and the internist advised operation. After seeing this patient

in the hospital I advised against operation, and recommended medical management, and after three weeks the niche disappeared, the symptoms were relieved, and the patient has remained well since that time (Fig. 2). The indication, therefore, for surgical intervention in the penetrating ulcer can be decided only by the clinical course, and not by the roentgenologic appearance of the lesion.

The patients who will not cooperate under medical management should not be operated upon. If one accepts this type of case as an indication for operation the results from any type of surgical procedure, whether it be a gastro-enterostomy or a subtotal resection, will be most unsatisfactory.

There is a great difference of opinion as to why we obtain good results in any surgical procedure for a duodenal ulcer. Perhaps the most generally accepted opinion is that it is due to a reduction in the gastric acidity, whether the operative procedure has been a gastro-enterostomy or a subtotal resection. We started 15 years ago to observe patients treated both medically and surgically, and to evaluate the reasons for failure in each group. We soon realized that a gastro-enterostomy undertaken for the adequately treated cases was very unsatisfactory. In our clinics at Bellevue Hospital we found that patients whom we were referring for gastro-enterostomy 12 to 15 years ago, constituting the intractable case with severe pain, obtained very poor results from surgery. The author personally had performed 29 gastro-enterostomies for duodenal ulcer in this group, and was amazed at the high percentage of failures from the short-circuiting procedure, so it was abandoned completely after 1932.

It is difficult, if not impossible, to evaluate the pathologic process in a duodenal ulcer unless a subtotal resection is done, and in the 29 gastro-enterostomies the ulcer was described as anterior in 14 instances, posterior in 13, and anterior and posterior in two instances. That is interesting when one evaluates 75 subtotal resections performed for duodenal ulcers in the same clinic, in which group there were 80 per cent posterior wall ulcers, with a definite chronic pancreatitis, in ten instances, or 13 per cent, there was both an anterior and a posterior wall ulcer, with pancreatitis, and in only five, or seven per cent, was there a single anterior wall ulcer. The ages of the patients in the two series were identical—37.1 per cent for the gastro-enterostomies, and 37.1 per cent for the subtotal resections. The symptoms in the gastro-enterostomies had persisted for 5.4 years and in the subtotal resections 5.3 years, which would indicate that we were treating, in all probability, identical ulcers.

The exact location of the duodenal ulcer is impossible to determine unless a subtotal resection has been performed. This point is illustrated in Figures 3, 4, 5 and 6.

Our opinion as to the best surgical procedure for intractable duodenal ulcer has been arrived at by evaluation of the results obtained from gastro-enterostomies performed in the stomach clinic of the Fourth Division of

INTRACTABLE DUODENAL ULCER

Bellevue Hospital, and reported⁸ in 1934, and again⁹ in 1940. From these reports conclusive evidence was produced to show that gastro-enterostomy was a most unsatisfactory method of treatment. In 1934 we reported 96 gastro-enterostomies, followed for an average of 4.2 years, with 37 per cent cures and 16.7 per cent gastrojejunal ulcers. In 1940 we reported 106 gastro-enterostomies, followed for an average of 7.1 years, with 24.5 per cent cures and 18.8 per cent gastrojejunal ulcers.

Since 1933 we have performed subtotal resections, exclusively, in all cases of duodenal ulcer. I am willing to admit that there is one indication for a gastro-enterostomy for duodenal ulcer, namely, the stenosing lesion which results from operative intervention for a previous acute perforation not associated with pain. Then a short-circuiting procedure should prove satis-

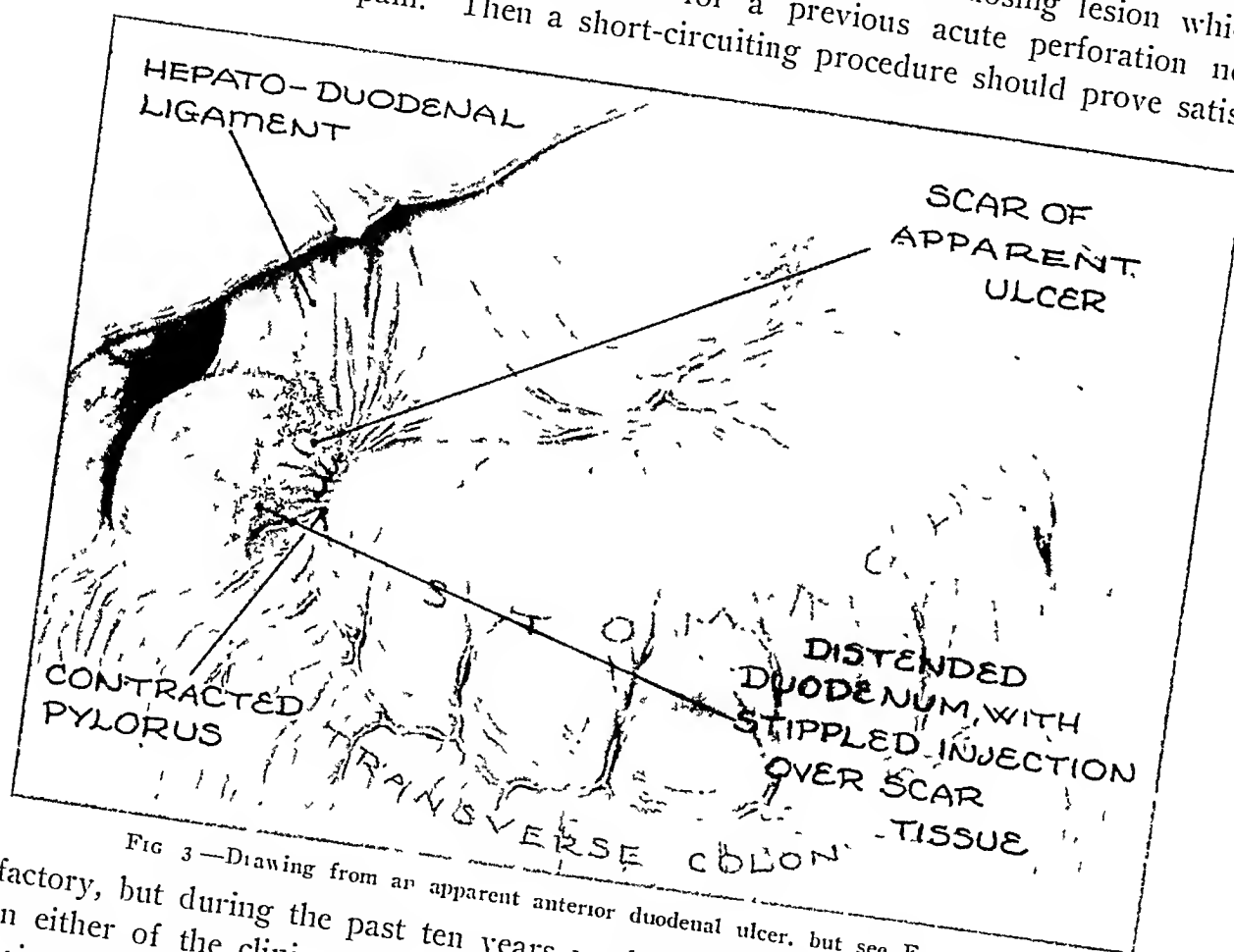


FIG 3—Drawing from an apparent anterior duodenal ulcer, but see Figure 4.

factory, but during the past ten years we have not encouraged such a case in either of the clinics with which I am associated, or in patients seen in private practice.

Subtotal resection is now accepted as the operative procedure for intractable duodenal ulcer. The term subtotal resection is rather loosely used, according to all recent writings, but the generally accepted concept merely means removal of one-half to three-fourths of the stomach, leaving *in situ*, if advisable, the pyloric end of the stomach and the duodenum with the adherent ulcer to the pancreas. Those who advocate leaving the good results ulcer and even the pyloric end of the stomach believe that the good results are based to a great extent, if not entirely, upon achlorhydria resulting from

subtotal resections. Little stress is placed upon ridding the patient of the inflammatory mass, which would seem to be essential in obtaining a good result.

Colp¹⁰ reported 502 subtotal resections, with 40 recurrences, and in 33 of the 40 the ulcer had been removed. He is definitely of the opinion that the removal of the ulcer has little to do with the recurrence and he goes on to state that the incidence of recurrence will be minimal in cases of anacidity but if free acid is present after operation the incidence of recurrence is going to be much greater. From my observations of patients in our clinics and in private practice, where the ulcer has been left *in situ* by other surgeons, there are more unsatisfactory results than in cases in which the ulcer has been removed *in toto*. A recent report¹¹ from our clinic at Bellevue Hospital shows that in none of the cases operated upon on our service, who have been followed, was a gastroduodenal ulcer found. In this group we had 104 subtotal resections followed on an average of 2.88 years, and these patients had made 1,822 visits, or 18 visits per patient. No case was reported which had not been followed for one year or longer. Sixty-five per cent of these patients were cured, which means they were completely symptom-free. Twenty-five per cent were improved, and the chief reason for placing them in this group was weight loss, without pain. The weight records in all cases of subtotal resections are interesting. In 47.6 per cent there was a weight loss, in 39.2 per cent the weight remained unchanged, and 8.4 per cent they lost and then gained weight.

If one accepts the teaching that achlorhydria is the goal to reach in subtotal resection, then there is a definite reason, in all instances, for removing the pylorus and the adherent ulcer. Experimental evidence shows that the mucosa of the pyloric end of the stomach affects the secretion from the cardia and fundus of the stomach by the hormone "gastrin," as shown by Edkins,¹² and Koch, Luckhard and Keston.¹³ These authors believe that the hormone is produced and thrown into the blood stream by the pyloric mucosa. Because of the similar action of histamine upon the gastric mucosa, several authors believe this hormone to be histamine. However, recent work on isolated and denervated gastric pouches with histamine-free extracts demonstrated the true hormone character of the internal secretion of the gastric mucosa.^{14, 15, 16}

There is little doubt that in those cases in which a subtotal resection of 50 to 75 per cent of the stomach is done and the duodenal ulcer is left *in situ*, the follow-up results are far from satisfactory. This point has been stressed by Friedell, Shaar and Walters,¹⁷ in which they state "while the prognosis as to ultimate cure and certainly as to the immediate relief is favorable, it surely does not present the same chance of a complete cure that pyloric removal does," and they cite a case in which the pyloric portion of the stomach and the duodenal region was not removed, but the gastric mucosa was dissected from the remaining pyloric stump. Analysis of the gastric con-

INTRACTABLE DUODENAL ULCER

tents three weeks after operation revealed 10 to 15 units of free hydrochloric acid in the gastric section which increased to 60 units after the administration of 0.5 mg. of histamine. They believed that neglecting to remove the pyloric portion of the stomach was a factor in the failure. Kiefer¹⁸ has elaborated upon this same point in reporting 222 subtotal resections for peptic ulcer. He emphasizes that 49 were for gastric lesion and 173 for duodenal ulcer. "In 30 cases, because of technical difficulties and their attendant risks, the duodenum and pylorus were not included in

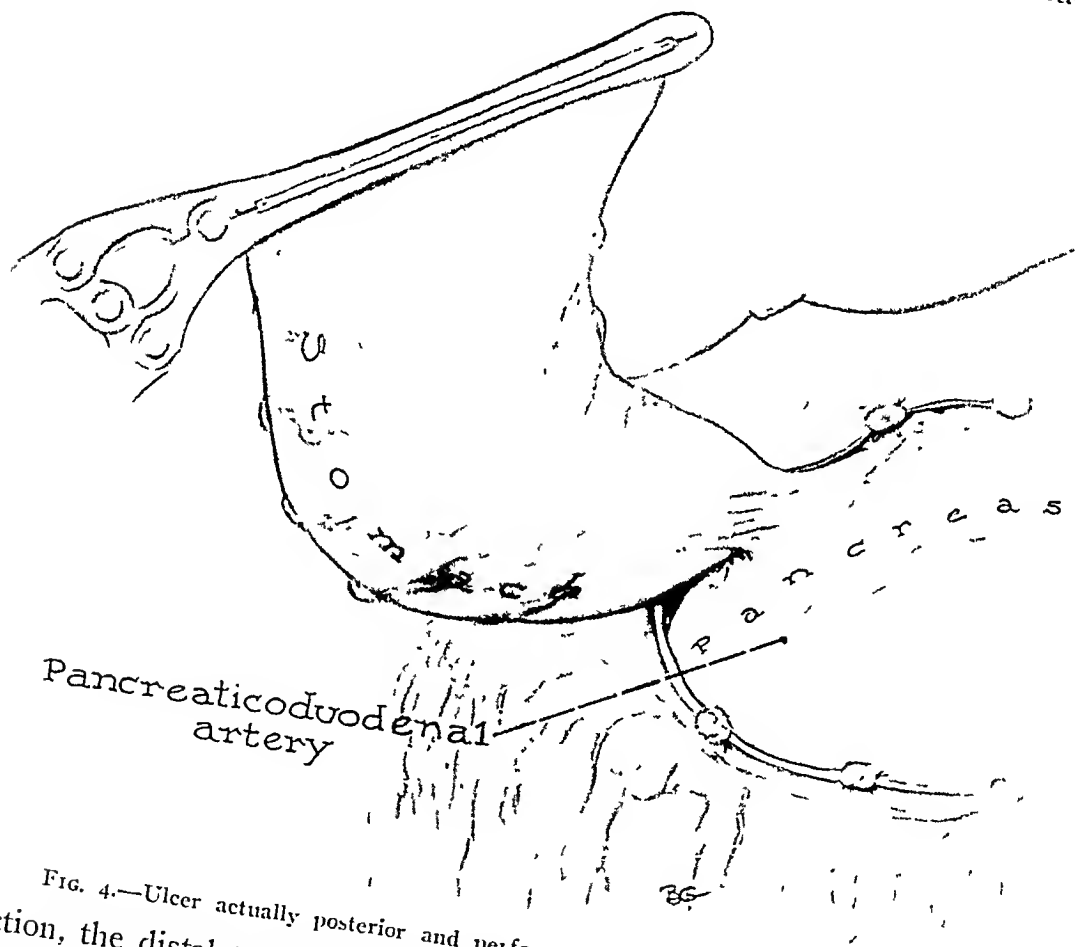


FIG. 4.—Ulcer actually posterior and perforating into head of pancreas.

the resection, the distal transection being placed proximal to the pylorus, as recommended by Finisterer in cases in which removal of the duodenum is too dangerous. In this group there were seven recurrent ulcers and three cases of postoperative hemorrhage. This relatively high incidence of unsatisfactory results has led to speculation regarding the rôle of the pylorus and the antrum since there is evidence that a hormone is evolved in the pars pylorica which stimulates the fundic glands to produce acid. However, actual evidence indicating that failure to remove the pyloric end of the stomach was solely responsible for the recurrence of the ulcer is rather meager. A post-operative gastric analysis after an Ewald meal was done in 24 cases of this group with the finding of free acid in 13 cases, which is approximately the same proportion as that found in the combined group

of duodenal ulcer cases. The fact that the surgeon had decided against the attempt to remove the pylorus was an indication that this group represented a particularly severe grade of peptic ulcer and might be expected to show a higher percentage of recurrence."

Whether or not a hormone is secreted by the pyloric end of the stomach, there seems to be little doubt, in some of the clinics with large experience with subtotal resections, that in those cases in which the duodenal ulcer is left *in situ* the results are not as satisfactory as when it is removed. The two previous reports vary as to their interpretation. One states that the result is due to increasing incidence of the acid; the other that it is due to a more virulent type of ulcerative process. If the latter opinion is correct, then there is every reason for removing such a lesion.

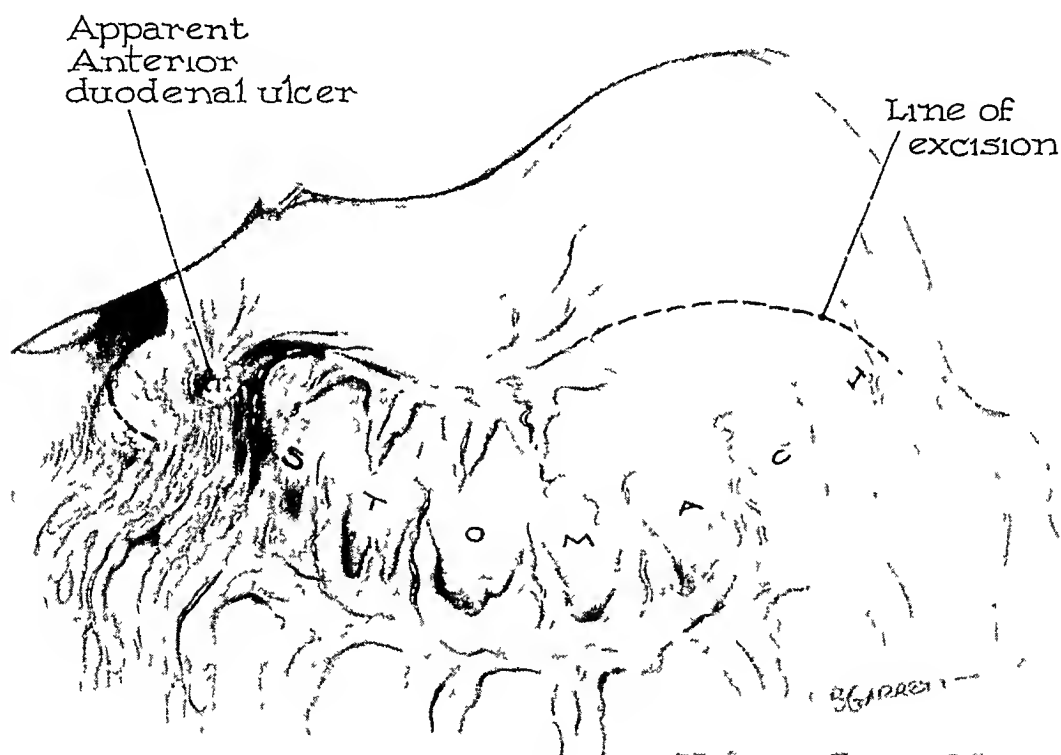


FIG 5—Apparent anterior duodenal ulcer, but see Figure 6

TECHNIC OF SUBTOTAL RESECTION

During the past ten years in every operation for duodenal ulcer, I have removed 65–70 per cent of the stomach, and the pylorus and the duodenal lesion *in toto*. One is constantly seeing in the literature statements to the effect that the lesion could not be removed due to the technical difficulties encountered. From my experience during the past ten years, which, in the clinics and private practice, includes over 150 cases, no case has been encountered in which the ulcer could not be removed. One of the very interesting phases of the so-called difficult lesion is the relative ease with which the apparently difficult ulcers were removed. Some of the smaller lesions are often much more difficult to remove technically than the large

INTRACTABLE DUODENAL ULCER

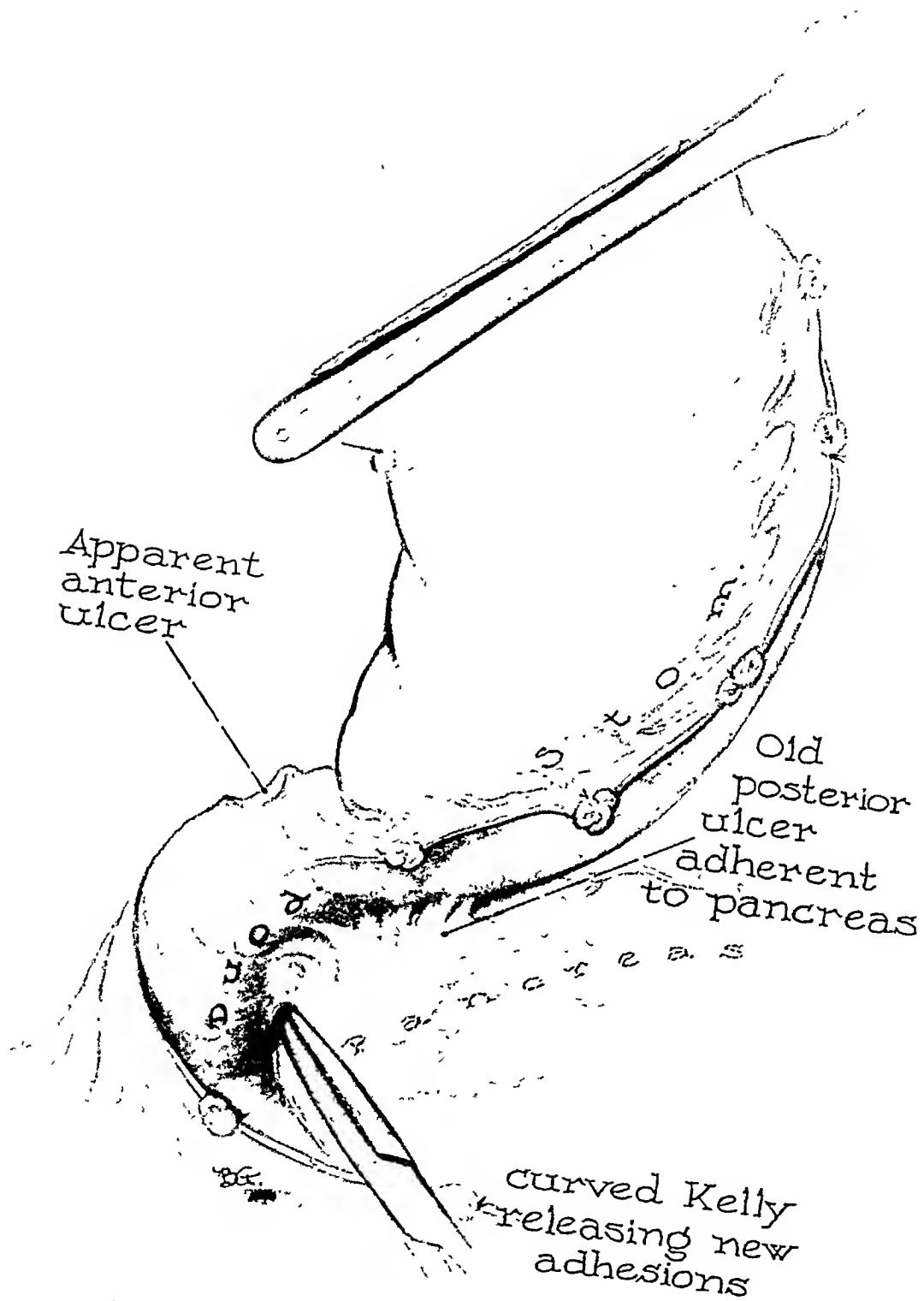


FIG. 6.—Ulcer posterior and perforating into head of pancreas.

inflammatory mass. The inflammatory process has completely occluded all the smaller vessels and the process is similar to removing the acutely inflamed gallbladder as compared with one subacutely or chronically inflamed. The former operation is technically much easier to perform. The same treat-

ment applies to the large inflammatory masses around the pancreas and duodenohepatic ligament.

The technic followed is to divide the gastrocolic omentum just proximal to the adherent mass and carry this proximally along the greater curvature to a point well above the reentrant angle of the stomach, after which the vessels in the gastrohepatic omentum are divided and then the stomach transected from right to left above the reentrant angle. This procedure provides an opportunity for exposing the adherent mass in the pancreas and duodenohepatic ligament and for freeing it under better visualization. After

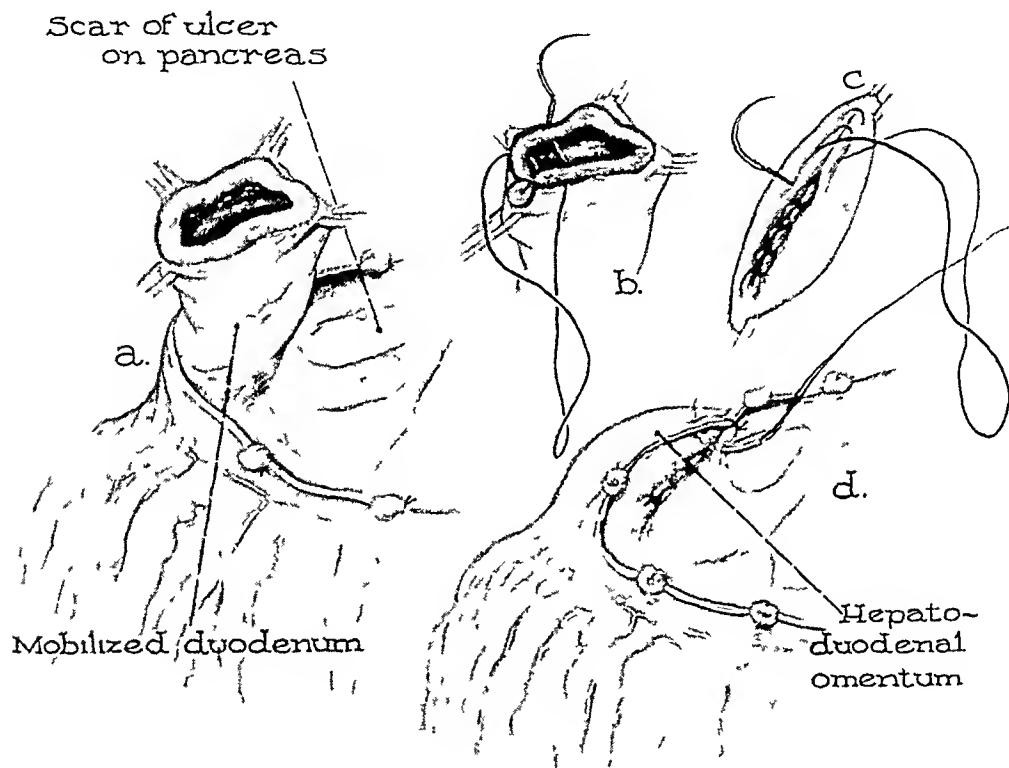


FIG 7—The duodenal ulcer can always be removed and the stump closed

the inflammatory mass has been completely separated, the duodenal stump is carefully closed with cotton sutures using four layers to completely invert the stump and bury it in the head of the pancreas in the region of the previous perforation (Fig. 7). The most important part of the whole operative procedure, as it affects mortality, is the closure of the duodenal stump. After this the continuity between stomach and jejunum is reestablished, as illustrated in Figure 8. Three layers of cotton sutures are used posteriorly and three layers anteriorly. The abdomen is always closed, without drainage, by using interrupted cotton sutures for the peritoneum, the fascia and the skin.

The preoperative care of ulcer patients is an important factor in their surgical management. In a previous report,¹⁹ pre- and postoperative physiologic balance was discussed, and the course of those patients operated upon on the Fourth Surgical Division at Bellevue Hospital evaluated. These

INTRACTABLE DUODENAL ULCER

patients averaged 17 days in the hospital preoperatively, and 19 days post-operatively. Although the majority had been under observation for years before operation was decided upon, this period gave us added time to further evaluate the severity of their pain and to completely restore their fluid balance

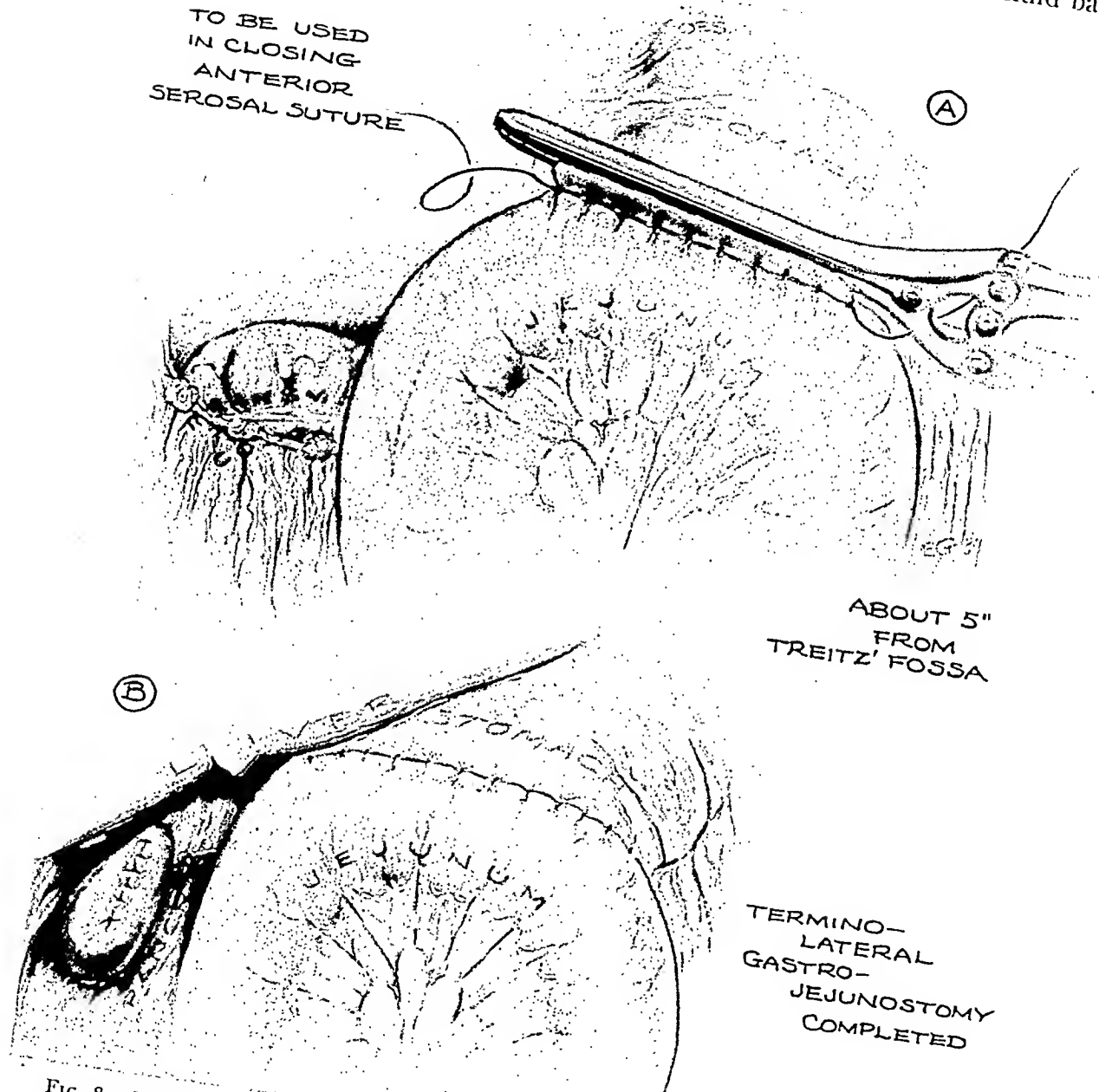


FIG. 8.—Method of performing an anterior short-loop anastomosis without entero-enterostomy.

and vitamin B and C deficiencies. They were always given 2,000 cc. of saline with 500 mg. of vitamin C and 100 mg. of vitamin B once a day for seven days preceding operation. Saline is used in preference to glucose, as the fluid remains in the tissues and does not have a diuretic action.

The type of anesthesia used has always been endotracheal, and the choice of the agent, whether it be cyclopropane or ether, or a combination of the two, is always left to the discretion of the anesthetist. Anesthesia in gastric

surgery has recently been reviewed by us.²⁰ Spinal anesthesia has not been used in any of the resections during the past ten years.

The postoperative management of these patients is important. Morphine should be used very sparingly. Large doses depress the respiratory tract, and, as Waters²¹ has aptly put it, "the cough reflex is eliminated which is the janitor of the respiratory tract." The patients are turned from side-to-side every hour. They are given an average of 5 mg. Magendi solution preoperatively and 15 mg. postoperatively. The Levine tube is passed one hour before operation, it is irrigated every hour postoperatively for 48 hours and left open for gravity drainage. Fluid is given by mouth as soon as the patient reacts, as it serves as a cleansing agent for gastric mucin. Postoperatively, the intravenous administration of fluid should be carefully watched as these patients are well hydrated preoperatively. During the first 24 hours, postoperatively, they should receive not more than 2,000 cc., and after 48 to 72 hours, intravenous administration of fluids may be discontinued.

In a previous report²² of operations at Bellevue Hospital, by the author, there were 102 subtotal resections for ulcer, with five deaths, one of which was attributed to pneumonia and the other four to peritonitis. Of the 102 patients, 33 had previously undergone gastric surgery. These cases, of course, are from a municipal hospital, without special nurses, and with all the other handicaps under which one works in taking care of major surgical cases in such an institution.

CONCLUSIONS

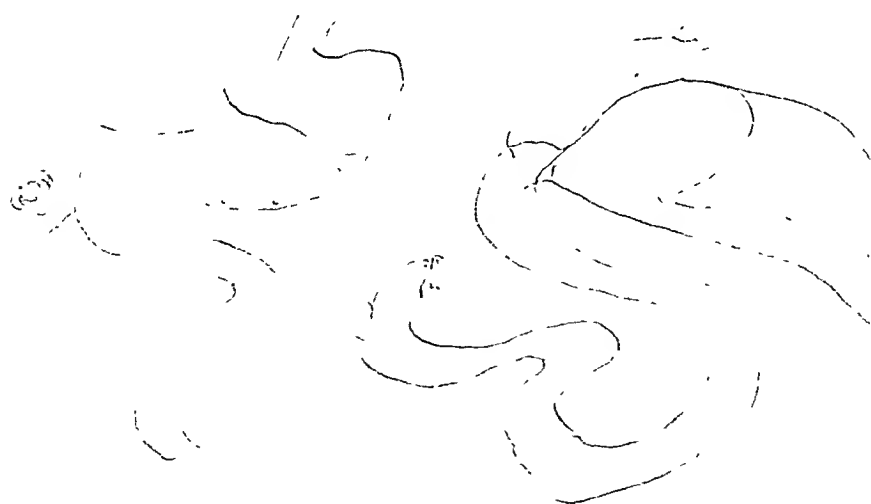
1. From my personal observation of a large number of chronic duodenal ulcers, I believe that the only indication for operation is uncontrollable pain which does not respond to any form of medical management.
2. When these patients are submitted to surgery, there is only one operative procedure which seems justifiable, namely, a subtotal gastrectomy, with removal of the pylorus and the ulcer *in toto*.
3. If the indications given above have been observed, gastrojejunal ulcer is a most uncommon occurrence following a subtotal resection.
4. Gastrojejunal ulcers will, of course, follow subtotal resections unless the patient has been given every chance under conservative management.

REFERENCES

- ¹ Allen, A. W.: Subtotal Gastrectomy for Stenosing Ulcer of Duodenum. J. A. M. A., 120, 493, October 17, 1942.
- ² Wilkinson, S. A.: Am. J. Dig. Dis., 9, 321, October, 1942.
- ³ Hinton, J. W.: Significance of Gross Hemorrhage in Peptic Ulcer. Am. J. Surg., N. S. 33, 180, August, 1936.
- ⁴ Hinton, J. W.: Massive Hemorrhage in Peptic Ulcer. ANNALS OF SURGERY, 110, 376, September, 1939.
- ⁵ Allen, A. W.: Surgery, 2, 713-731, November, 1937.
- ⁶ Blackford, J. M., and Cole, W. S.: Am. J. Dig. Dis., 6, 637-641, November, 1939.

INTRACTABLE DUODENAL ULCER

- ⁷ Blackford, J. M., and Allen, H. E.: Bleeding Peptic Ulcers. *J. A. M. A.*, **120**, 811-812, November 14, 1942.
- ⁸ Church, R. E., and Hinton, J. W.: A Study of 671 Cases of Peptic Ulcer: With Special Emphasis on 114 Postoperated Cases. *N. Y. State J. Med.*, **34**, 1079, December 15, 1934.
- ⁹ Church, R. E., and Hinton, J. W.: The Results of Gastro-enterostomy in Gastric and Duodenal Ulcers. *Surg. J.*, **7**, 647-656, May, 1940.
- ¹⁰ Colp, R.: *Am. J. Dig. Dis.*, **9**, 324, October, 1942.
- ¹¹ Church, R. E., and Hinton, J. W.: Follow-up Results in Subtotal Gastric Resection for Ulcers. *Am. J. Dig. Dis.*, **9**, 317, October, 1942.
- ¹² Edkins, J. S.: The Chemical Mechanism of Gastric Secretion. *J. Phys.*, **34**, 133-144, 1906.
- ¹³ Koch, F. C., Luckhardt, A. B., and Keston, R. W.: Gastrin Studies: V. Chemical Studies on Gastrin Bodies. *Am. J. Phys.*, **52**, 508, 1920.
- ¹⁴ Friedman, M. H. F.: The Influence of Glucose Administration on Gastric Secretion. *Am. J. Phys.*, **126**, 495, 1939.
- ¹⁵ Babkin, B. P.: The Triple Mechanism of the Chemical Phase of Gastric Secretion. *Am. J. Dig. Dis.*, **5**, 467, 1938.
- ¹⁶ Best, C., and Taylor, N.: *Physiological Basis of Medical Practice*. Baltimore, Williams and Wilkins Co., ed. 2, p. 690, 1939.
- ¹⁷ Friedell, M. T., Shaar, C. M., Walters, W.: Effect of Gastric Resection on Gastric Acidity. *J. A. M. A.*, **120**, 666, October 31, 1942.
- ¹⁸ Kiefer, E. D.: Jejunal Ulcers and Recurrent Hemorrhages After Gastrectomy for Peptic Ulcer. *J. A. M. A.*, **120**, 819, November 14, 1942.
- ¹⁹ Hinton, J. W., and Phelps, McK.: The Preoperative and Postoperative Physiologic Balance of Ulcer Patients. *Med. Clin. of No. Am.*, **26**, No. 3, 677-681, May, 1940.
- ²⁰ Phelps, McK., Hinton, J. W., and Rovenstine, E. A.: Anesthesia During Subtotal Gastrectomy. *Am. J. Surg.*, **N. S. 58**, 198, November, 1942.
- ²¹ Waters, R. M.: Anoxia: The Anesthetist's Point of View. *J. A. M. A.*, **115**, 1687, November 16, 1940.
- ²² Hinton, J. W., and Church, R. E.: Selection of Operation in Gastric and Duodenal Ulcer. *J. A. M. A.*, **120**, 816, November 14, 1942.



NITROGEN METABOLISM, CALORIC INTAKE AND WEIGHT LOSS IN POSTOPERATIVE CONVALESCENCE*

A STUDY OF EIGHT PATIENTS UNDERGOING PARTIAL GASTRECTOMY
FOR DUODENAL ULCERS

JOHN H. MULHOLLAND,† M.D., CO TUI, M.D., ARTHUR M. WRIGHT, M.D.,
AND VINCENT J. VINCI, M.D.

NEW YORK, N. Y.

FROM THE DEPARTMENT OF SURGERY, AND LABORATORY OF EXPERIMENTAL SURGERY, NEW YORK UNIVERSITY
COLLEGE OF MEDICINE; AND THE NEW YORK UNIVERSITY SURGICAL DIVISION OF BELLEVUE HOSPITAL, N. Y.

THE SCIENCE OF NUTRITION has not until recently engaged the serious attention of the surgeon. This is attributable to several factors. The nausea and vomiting, the impairment of appetite and the derangement of digestive processes caused by anesthesia, and the pain and the emotional stress connected with an operation, and by the operation itself, are not conducive to healthy alimentation. Added to this may be mentioned the fear on the part of the surgeon of placing food into a viscus which has been the site of a recent operation. However, since the usual surgical case requires dietetic restriction only for a few days postoperatively, and since most patients come to operation with enough body stores to tide them over this lean period, the surgeon has rarely been impelled to regard nutrition as a matter of any urgency.

The work on the rôle of hypoproteinemia in surgical conditions by Jones, and his coworkers,¹ Ravdin, and his associates,^{2, 3} Koster and Shapiro,⁴ and Hartzell, and his coworkers,⁵ the study by Cuthbertson,⁶ in England, of nitrogen loss, sometimes called the "toxic loss of nitrogen," and by Elman,⁷ and Brunschwig, *et al.*,⁸ in this country, and the demonstration by these last two workers of the safety and feasibility of intravenous alimentation, constitute a new chapter in surgery. The work of these men has, at last, linked surgery with the basic work of pioneers like Van Slyke, Rose, Whipple, Madden, Weech and others.

While it is true that most surgical patients need little nutritional attention, there are surgical conditions in which the maintenance of the nutritional state is a matter of grave importance. One of these conditions is peptic ulcers. Thus, Riggs, Reinhold, Boles and Shore⁹ found statistically significant deficiencies in serum total protein, albumin and vitamin C concentrations in a group of 52 cases of peptic ulcer. Many of these ulcer patients, either as a result of dieting or of repeated bleeding, have lost considerable weight, with the blood protein at or below the lower limit of normal, and the body stores well depleted. Some lend themselves to preoperative "building up,"

* Under a grant from Mead-Johnson Co.

† Professor of Clinical Surgery New York University College of Medicine, and now Lt. Col., M. C., U. S. A.

POSTOPERATIVE METABOLISM

but others may require emergency operations while in their depleted state. If a major operation, such as gastrectomy, is performed upon these patients, there is added to the "toxic loss of nitrogen" the partial starvation imposed by a highly restricted postoperative regimen, which further depletes the body tissues, interferes with healing, and may lead to wound dehiscence. An example of this is D. R., reported in Table I.

In the present study the nitrogen balance was determined in eight cases of duodenal ulcers who had undergone partial gastrectomy. They were divided into two groups: four cases who were given the postoperative ward routine of infusions, occasional blood transfusions, and a gradually increasing oral feeding. This may be called the control group. In the other group of four cases, a high caloric and high nitrogen feeding was given to replace or more than replace the nitrogen loss, so that at the end of the postoperative period of 10 to 12 days, a nitrogen surplus was accumulated in the body. In addition to the nitrogen balance, both the body weight and the plasma proteins in both groups were determined periodically throughout the convalescent period. The fluid intake and output were followed and the caloric and sodium chloride intakes were noted. The chief sources of nitrogen loss were recorded. Also noted, but not objectively studied, was the "strength" of the patient. The number of days of hospitalization of one group was compared with that in the other. Tables V to VIII each a high nitrogen feeding case. Graphs a, b, c and d in Figure 1 are records of the control group, and corresponding graphs in Figure 2, of the feeding group, showing the important representative findings.

EXPERIMENTAL CONSIDERATIONS

Preoperative Preparation of the Patient.—The patients in the control group each had a Levin tube introduced through one of the nares into the stomach for decompression of this viscus by the Wangensteen suction apparatus during the first four to six postoperative days. In the feeding group the Levin tube was replaced by a double-lumen tube, adopted from "a Miller-Abbott tube in such a way that one barrel was longer than the other by some ten inches. The shorter barrel was for suction and the longer for feeding. The ends of both barrels were perforated at several levels, in order to facilitate feeding and suction. During the operation, after the stomach was resected, and while the anastomosis was being made, the feeding barrel was introduced through the stoma into the jejunum, after which the operative routine was resumed. Immediately postoperatively, Wangensteen suction was made through the suction barrel, which lay in the stomach. *The Weight of the Patient.*—The weights of the patients were taken on the Howe platform scales. In the case of preoperative weights it was a simple matter for the patients simply stood on the scale platform for the weighing. In the postoperative period, however, the matter of weighing was somewhat more complicated. If the patient was light: *i.e.*, not over 60

Kg., he was lifted by an orderly and the weights of both the orderly and the patient were taken, after which the weight of the orderly was then subtracted from the combined weight. If he was over 60 Kg., he was placed on a stretcher and the loaded stretcher was then weighed on two scales, the two front wheels on the platform of one scale and the hind wheels over that of another. The two scales used in this work were sensitive to within 25 Gm., so that where two scales were used, the sensitivity would be decreased by half, and the margin of error would be in the neighborhood of 50 Gm. Since it was not the absolute weight but the comparative readings taken over several weighings for the construction of the weight curve, which was important, this margin of error was not serious.

The Fluid Intake.—In the control group, the fluid intake was maintained mainly by intravenous infusions of 5 or 10% dextrose solutions in distilled water or in physiologic saline, some for the first four or five days and some for a longer period. Occasionally amigen solution was also given intravenously. The amount lost by gastric suction was replaced by a corresponding amount of saline, according to Coller and Maddock's¹⁰ principle. This accounts for the large fluid and NaCl intake of the first four to six days in both groups. After the first four or five days, when fluid intake by mouth was being gradually increased, the infusions were tapered off correspondingly.

In the feeding group, the first two cases (A. V., Table V and F. R., Table VI) had a large number of intravenous infusions. In the last two cases, however, infusions were given only in the first postoperative 12 hours and thereafter the fluid intake was entirely given through the feeding tube or by mouth.

The Chloride Intake.—An attempt was made not to exceed the chloride intake of nine grams daily. However, the problem was complicated by the loss of fluid through the gastric suction. As stated above, the Coller and Maddock¹⁰ principle required this amount to be replaced quantitatively in physiologic saline, and this accounts for the apparently unduly large amount of sodium chloride the first four to six days. However, a possible source of error is present in this volume-for-volume replacement. If the suction were continued while the patient took a drink of water, the drainage might contain less sodium chloride than was assumed in the Coller and Maddock principle and, consequently, the patient would be given more sodium chloride than he needed. In order to obviate this, the suction was turned off for half an hour after each drink. Whether in this time the water had all passed out of the stomach or become isosmotic with systemic fluids is not known.

The Caloric and Nitrogen Intakes.—In the control group, the caloric intake was derived from three sources: (a) Infusion of dextrose solutions, four calories being assigned to each gram of dextrose; (b) peptonised milk and the usual articles of soft diet, the caloric and nitrogen values of which were taken from the dietitians' chart; and (c) the few calories and small amount of nitrogen derived from the plasma proteins in the blood trans-

POSTOPERATIVE METABOLISM

TABLE I
CASE OF D. R., MALE, AGE 50

TABLE I														
CASE OF D. R., MALE, AGE 50														
Date	Fluid Output			—N—Output										
	Fluid Intake Cc.	Gastric Suction Cc.	Urinary Vol. Cc.	Chloride Intake Gm.	Cl. Intake	N Intake Gm.	Urinary N Gm.	Gastric N Gm.	Fecal N Gm.	Total N Output Gm.	N Balance Gm.	Cum. N Status Gm.	P.P. Gm. % A/G	Wt. Kg.
March 8	3250	980	1300	20.25	870	2.8	7.983	.809	.593	9.466	-6.666	-6.666	3.25.4	63.4
9 to 10	3000	750	1200	18	1140	5.6	15.877	.771	.593	17.241	-11.641	-18.307		
10 to 11	3000	860	1000	9	800	0	10.995	5.656	.593	-17.244	-17.244	-35.551		
11 to 12	3000	960	1050	9	800	0	6.227	7.665	.593	14.485	-14.485	-50.036		
12 to 13	3000	920	1240	18	800	0	7.583	1.297	.593	9.473	-9.473	-59.509		
13 to 14	3250	1050	1100	18	800	0	8.142	2.5	.593	11.235	-11.235	-70.744		
14 to 15	3500	700	850	9	940	5.6	17.028	3.559	.593	21.18	-15.58	-86.324		
15 to 06	2500	0	940	5.6	17.028	3.559	.593	.593	.593	59.15	Inf. as above. H ₂ O by mouth to volume.			
16 to 17	2250	0	1150	9	870	2.8	13.354	—	.931	14.285	-11.485	-97.809		
17 to 18	3820	—	1342	9	1231	6.97	6.886	—	.931	7.817	—	.847	-98.656	
18 to 19	2200	—	855	9	1342	6.342	14.115	—	.931	15.046	-8.704	-107.360		
19 to 20	3000	—	1107	11.88	6.342	12.142	—	.931	13.073	-6.731	-114.091	5.20		
Total	6220	887	1107	11.88	6.342	12.142	—	.931	13.073	-6.731	-114.091	5.20		
Average	6220	887	1107	11.88	6.342	12.142	—	.931	13.073	-6.731	-114.091	5.20		
20—on soft diet + 500 cc. nutriment.	36.454	120.332	22.25	7.875	-150.545	5.20	56.45							
4—2	3.314	10.939	3.18	.716	-13.686									
April 13														

6.17 61 Wound begins healing March 24.
6.65 62.5 Discharged. Wound partially healed.

TABLE II
CASE R. B., MALE, AGE 33

Date	Fluid Output			—N—Output							Wt. Kg.	Remarks			
	Intake Cc.	Gastric Cc.	Urinary Vol. Cc.	Cl Intake Gm.	Caloric Intake Gm.	N Intake Gm.	Urinary		Fecal N Gm.	Total N Output Gm.			N Balance Gm.	Cum. N Status Gm.	P.P. Gm. % A/G
							N Gm.	Gm.							
May 11															
12 to 13	3250	450	1700	13.5	670	2.8	11.909	.841	.351	.351	13.106	—10.306	—10.306	6.15	64.32
13 to 14	3850	920	1725	16.65	1468	6.92	16.917	1.113	.351	.351	18.381	—11.461	—21.767		500 Tr. W.B. Inf. 1L. 5% dex. in saline; 2L. in D/W.
14 to 15	3500	450	2200	13.5	1340	5.6	14.9	.330	.351	.351	15.581	— 9.981	—31.748	5.64	61.6
15 to 16	3250	1800	2000	11.25	870	5.6	16.812	1.975	.351	.351	19.138	—13.538	—45.286		Tr. 350 cc. plasma. Inf. 500 cc. 5% amigen in 5% dex.; 2L. 10% dex. in D/W; 1L. ditto in saline.
16 to 17	3250	0	2200	11.25	1210	8.8	17.757	—	.351	.351	18.108	— 9.308	—54.594		Tr. 500 cc. W.B.; 250 cc. plasma. Inf. 2L. 10% dex. in D/W; 1L. in saline.
17 to 18	2690	0	1800	13.25	1154	11.123	16.757	—	.351	.351	17.108	— 5.985	—60.579	60.68	Tr. 500 W.B.; 1L. 10% dex. in saline. 2L. 5% dex. in D/W.
18 to 19	2660	0	1500	5.94	1271	3.489	15.64	—	.351	.351	15.991	—12.502	—73.081		Tr. 250 cc. plasma; Inf. 1000 cc. 5% amigen; 2L. 10% dex. in D/W.
19 to 20	1880	0	1650	7.92	692	4.646	13.42	—	.351	.351	13.771	— 9.125	—82.206	5.52	60.00
Total	3620					48.978	124.212	3.259	2.808	2.808	131.184				Tr. 250 cc. plasma; Inf. 2L. 5% amigen in 5% dex. 1L. 10% dex. in D/W. 440 cc. pep. milk.
Average	905					6.123	15.462	.815			16.398				Inf.—2L. 10% dex. in D/W.
20—on Sippy diet + 500 Gm. nutramigen.															4 cups tea with 1 teaspoonful sugar each. 880 cc. pep. milk.
June 3															
June 5														7.01	64.3
															64.8
															Discharged.

500 Tr. W.B. Inf. 1L. 5% dex. in saline; 2L. in D/W.
Tr. 350 cc. plasma. Inf. 500 cc. 5% amigen in 5% dex.; 2L. 10% dex. in D/W; 1L. ditto in saline.
Tr. 500 cc. W.B.; 250 cc. plasma. Inf. 2L. 10% dex. in D/W; 1L. in saline.
Tr. 500 W.B.; 1L. 10% dex. in saline. 2L. 5% dex. in D/W.
Tr. 250 cc. plasma; Inf. 1000 cc. 5% amigen; 2L. 10% dex. in D/W.
Tr. 250 cc. plasma; Inf. 2L. 5% amigen in 5% dex. 1L. 10% dex. in D/W. 440 cc. pep. milk.
Inf.—2L. 10% dex. in D/W.
4 cups tea with 1 teaspoonful sugar each. 880 cc. pep. milk.

POSTOPERATIVE METABOLISM

TABLE III
CASE F. W., MALE, AGE 50

Date	Fluid Output			N—Output				Cum. N. Status Gm.	P.P. Gm. % A/G	Hem. Kg.	Wt. Kg.	Remarks
	Intake Cc.	Gastric Intake Cc.	Urinary Vol. Cc.	Caloric Intake Gm.	N Intake Gm.	Urinary N Gm.	Gastric N Gm.	Fecal N Gm.	Total N Output Gm.	N Balance Gm.		
Dec. 13	4250	880	1630	18	1010	14.8	11.944	.642	.692	13.278	+ 1.322	4.1/2.4 25 57.97
14 to 15	3660	450	1500	9	600	0	10.964	.135	.692	11.791	- 11.791	Tr. 500 cc. W.B. Inf. 2L. 5% agimen and 5% dex. 1L. 5% dex. in 1L. saline.
15 to 16	2050	400	1500	0	80	0	.150	.692	.692	11.791	- 10.269	2L. 5% dex. in saline. 1L. 5% dex. in H ₂ O; H ₂ O by tube = 660 cc.
17 to 18	2050	440	3550	0	80	0	.137	.692	.692	26.173	- 22.156	600 cc. tea with 80 Gm. sugar.
18 to 19	2050	1230	1230	0	700	0	.692	.692	.692	5.35	31	1450 cc. H ₂ O.
19 to 20	?	875	?	850	?	?	?	?	?	5.35	31	Ditto.
20 to 21	1000	1000	1000	850	17.123	23.754	.692	.692	.692	25.830	- 8.707	760 cc. pep. milk + H ₂ O + broth.
21 to 22	1375	1375	1375	850	23.67	24.639	.692	.692	.692	1080 cc. pep. milk + broth + H ₂ O.	55.68	
22 to 23	1250	1250	1250	1130	6.5	6.429	.692	.692	.692	Ditto.	Ditto.	
23 to 24	700	700	700	1900?	23.67	24.639	.692	.692	.692	- 3.045	- 44.177	
24 to 25	1400	1400	1400	1900?	6.5	6.429	.692	.692	.692	7.121	- .621	
25 to 26	1350	1350	1350	1900	66.110	126.16	1.064	8.304	110.908	- 44.798	6.8	Soft diet (partially consumed).
26 to 27					5.509	18.025	.216	.692	9.242		39	Soft diet (partially consumed).
27 to 28											53.52	Soft diet (partially consumed).
Total	2170											
Average	543											
Jan. 3												Discharged.

Discharged.

TABLE IV
CASE J. S., FEMALE, AGE 48

Date	Fluid Output			Cl. Intake Gm.	Caloric Intake	N Intake Gm.	-N--Output				Total N Output Gm.	N Balance Gm.	Cum. N Status Gm.	P.P. Gm. % A/G	Wt.		Remarks
	Intake Cc.	Gastric Cc.	Urinary N Gm.				Gastric N Gm.	Fecal N Gm.	Hem.	Kg.							
Dec. 9														7.48	43	85.23	
10 to 11	2530	1000	830	45	940	5.6	7.538	4.67	.22	12.448	—	6.848	—	6.848			In 1L. W.B.; 2L. 10% dex. in D/W.
11 to 12	3300	2650	725	9	1200	0	6.886	25.368	.22	22.474	—	22.474	—	29.322			Inf. 3L. 10% dex. in D/W; 300 cc. H ₂ O by tube.
12 to 13	3050	1600 (bloody)	930	18	800												Inf. 2L. 10% dex. in H ₂ O; 300 cc. H ₂ O by tube.
13 to 14	3150	2650 (bloody)	850	9	600	0	37.58	39.368	.659	83.538	—	83.538	—	112.86			600 cc. H ₂ O + 450 cc. tea.
14 to 15	2800	1650	680	9	400												Inf. 1L. 5% dex. in saline; 1L. 10% dex. in H ₂ O; 1150 cc. H ₂ O and tea.
15 to 16	?	—	950	?				0						81.81			Inf. 2L. 5% dex. in H ₂ O; 1L. in saline; 800 cc. H ₂ O and tea.
16 to 17	?	—	1200	?	2220	14.27	41.87	0	.659	42.529	—	28.259	—	141.119	6.34	38	4 glasses pep. milk; water and tea to 2500 cc.
17 to 18	?	—	1100	?	?			0							6.12	37	5 glasses pep. milk; H ₂ O and tea.
Total		9550				19.87	93.894	69.406	1.738	160.989							4½ glasses pep. milk; H ₂ O and tea.
Average		1950				3.974	11.737	17.451	.21	20.125							
18—On soft diet.																	
21																	81.36
27														6.54	38	81.36	Discharged.
Dec. 27																	

TABLE V
CASE A. V., MALE, AGE 47

Date	Fluid Output			—N—Output					N. Deficit or Surplus	P.P. Gm. % A/G	Hem. Kg.	Wt. Kg.	Remarks			
	Fluid Intake Cc.	Gastric Suction Cc.	Urinary Vol. Cc.	Cl Intake Gm.	Caloric Intake Gm.	N Intake Gm.	Urinary N Gm.	Gastric N Gm.						Fecal N Gm.	Total N Output Gm.	N Balance Gm.
Mar. 31																
April																
1 to 2	2250	825	650	11.25	470	2.8	3.764	2.100	.965	6.829	-4.029	- 4.029		Tr. 500 cc. W.B. 1L. 5% dex. in saline; 1L. ditto in D/W.		
2 to 3	3800	1500	1050	13.50	4025	20.25	8.9	1.576	.965	11.441	+8.809	+ 4.78		750 Gm. nutramigen by mouth in 1500 cc. saline—water to make 3800 cc. Inf. 1L. 5% dex. in D/W.		
3 to 4	4500	2600	700	18	4025	20.25	13.207	3.036	.965	17.208	+3.042	+ 7.82	69.8	Ditto—with 2000 cc. saline and H ₂ O to make 4500 cc.		
4 to 5	4500	2800	1000	18	4025	20.25	10.6	2.615	.934	14.149	+6.101	+13.923	6.72	Ditto—with 2000 cc. saline and H ₂ O to make 4500 cc. Inf. 1L. 5% dex. in D/W.		
5 to 6	4500	1700	1150	18	4025	20.25	10.787	1.667	.941	13.395	+6.855	+20.778	70.5	Ditto—with 2500 cc. saline and H ₂ O to make 4500 cc. Inf. 1L. 5% dex. in D/W.		
6 to 7	3000		1900	18	4025	20.25	10.796		.941	11.737	+8.513	+29.291		Ditto—with 2000 cc. saline and H ₂ O to make 3000 cc. Inf. 1L. 5% dex. in D/W.		
7 to 8	3000		1400	9	4025	20.25	10.358		.941	11.299	+8.951	+38.242	7.17 70.91	Ditto—with 1000 cc. saline and H ₂ O to make 3000 cc. Inf. 1L. 5% dex. in D/W.		
Total						124.3	68.412	10.994	7.691	86.303						
Average		1121				17.757	9.773	2.199	1.099	12.329						
Apr. 19														Discharged.		

TABLE VI
CASE F. R., MALE, AGE 55

Date	Fluid Output				-N-Output							Cum. N. Status Gm.	P.P. Gm. % A/G Hem.	Wt. Kg.	Remarks	
	Gastric		Urinary	N	Calorie	Cl	Gastric		Fecal	Total N						
	Intake	Suction					Vol.	Intake			N					Intake
June 5 8 to 9	3250	2100	1700	11.25	1270	2.8	20.403	7.355	.254	28.012	-25.212	-25.212	6.76	46.5	48.2	Tr. 500 cc. W.B. with re- action. Inf. 2L. 10% dex. in D/W; 1L. ditto, in saline.
9 to 10	4000	1810	1600	27.0	1370	6.0	11.021	3.297	.254	14.572	- 8.572	-33.784				Inf. 1L. 10% dex. in D/W; 2L. ditto. in saline; 1L. 5% amigen.
10 to 11	4500	2010	840	22.5	4090	22.385	8.767	9.856	.254	18.877	+ 3.508	-30.276	6.12	38	46.9	2L. 10% dex. in saline; 700, Gm. nutramigen in 500 cc. saline; H ₂ O to make total 2500 cc.
11 to 12	4500	2000	1300	22.5	4320	27.031	7.5	3.736	.254	11.490	+15.541	-14.735				Inf. 1L. 10% dex. in D/W; 700 Gm. nutramigen in 880 cc; pep. milk; water to make 4500 cc.
12 to 13	4000	1200	1000	16.92	4320	27.031	8.172	2.382	.254	10.808	+16.223	+ 1.488				Inf. 1L. 10% dex. in D/W; 700 Gm. nutramigen in 880 cc. pep. milk; H ₂ O to make 4L. 750 Gm. nutramigen in 880 cc. pep. milk; water to make 3½L.
13 to 14	3500	—	1250	7.92	4155	28.385	8.64	—	.887	9.527	+18.858	+20.346				Ditto—water to make 3L.
14 to 15	3000	—	1050	7.92	4150	28.385	7.835	—	.887	8.722	+19.663	+40.009	6.58	44	48.73	
15 to 16	3000		980	7.92	4150	28.385	7.64	—	.887	8.527	+19.858	+59.867				
16 to 17	3000		1100	7.92	4150	28.385	9.751	—	.895	10.646	+17.739	+77.606				
17 to 18	3000		1250	7.92	4150	28.385	8.642	—	.895	9.537	+18.848	+96.454				
18 to 19	3000		1040	7.92	4150	28.385	8.96	—	.895	9.855	+18.530	+114.984	6.84	46	52.15	
Total		9120				255.557	107.331	26.626	6.616	140.573						
Average		1824				23.222	9.766	5.325	.601	12.779						Discharged.
June 25																

POSTOPERATIVE METABOLISM

TABLE VII
CASE V. B., MALE, AGE 39

Date	Fluid Intake			Fluid Output			N—Output			Cum. N. Status Gm.	P.P. Gm. % A/G	Hem. Kg.	Wt. Kg.	Remarks
	Intake Cc.	Gastric Intake Cc.	Urinary Intake Cc.	Caloric Intake Gm.	N Intake Gm.	Urinary N Gm.	Gastric N Gm.	Fecal N Gm.	Total N Output Gm.					
Nov. 10	4500	950	900	13.5	3053									
11 to 12	3500	1250	1180	18	3630									
12 to 13	3500	1150	1200	18	3630									
13 to 14	3000	650	860	9	3630									
14 to 15	3000	450	800	9	3630									
15 to 16	3000	400	860	9	3630									
16 to 17	3000	—	940	9	3630									
17 to 18	3000	—	800	9	3360									
18 to 19	3000	—	1400	9	4230									
19 to 20	3000	—	1000	9	4700									
20 to 21	3000	—	1000	9	4700									
21 to 22	3000	—	1000	9	4700									
22 to 23	3000	—	1700	9	4700									
Total	4850	—	—	—	—	—	—	—	—	—	—	—	—	—
Average	808	—	—	—	—	—	—	—	—	—	—	—	—	—

TABLE VIII

CASE P. F., MALE, AGE 41

Date	Fluid Output				—N—Output										Remarks	
	Gastric		Urinary	N Intake	Caloric Intake	N Intake	Gastric		Fecal	Total N Output	N Balance	Cum. N. Status	P.P.			
	Intake	Suction					Cc.	Cc.					N	Gm.		Gm.
Dec. 2																
3 to 4	4500	2400	15	5	31.5	3440	71.2	52.089	10.308	1.26	66.177	+ 5.023	+ 5.023	4.47	2.7	50 51.47
																500 cc. W.B. (severe reaction) + 1L. 5% amigen; 1L. 10% dex. in saline + 600 Gm; nutramigen + 100 Gm. amigen in 1.5L. saline. Water to make 2.5L.
4 to 5	4500	2270	1620		27	3330				1.26				6.8	43	600 Gm. nutramigen; 150 Gm amigen in 3L. saline; H ₂ O to make 4500 cc.
5 to 6	4500	2140	1060		27	3330				1.26						Ditto.
6 to 7	4500	2070	950		27	3330	88.65	65.059	10.462	1.26	79.301	+ 9.349	+ 14.372		51.81	Ditto.
7 to 8	4500	2370	970		27	4035				1.26						750 Gm. nutramigen; 150 Gm. amigen + 3L. saline + H ₂ O to make 4500 cc.
8 to 9	4500	2450	1525		27	4035			5.154	1.26		+ 45.213	+ 59.585			Ditto; water to make 3500 cc.
9 to 10	3500	0	1120		9	4035	114.75	60.603		1.26	69.537					Ditto; amigen + nutramigen in 1L. saline; H ₂ O to make 3500 cc.
														6.7	41	Ditto.
10 to 11	3500	0	1650		9	4035				1.26						Ditto.
11 to 12	3500	0	1050		9	4035				1.26						Ditto.
12 to 13	3500	0	1500		9	4035	153	83.99		1.26	89.030	+ 63.970	+ 123.555			Ditto.
13 to 14	3500	0	1650		9	4035				1.26						Ditto.
14 to 15	3500	0	1250		9	4035				1.26				6.81	42	Ditto.
Total							427.60	61.741	25.924	15.12	304.045					Ditto.
Average							35.633	21.811	4.154		25.337					Discharged.
Dec. 16																

POSTOPERATIVE METABOLISM

fusions, assuming that the total protein concentration was uniformly 7 Gm. per cent. Five hundred cubic centimeters of whole blood would thus yield about 250 cc. of plasma, which would contain 17.5 Gm. of proteins, equivalent to 70 calories and 2.8 Gm. of nitrogen. The protein contained in the hemoglobin of the transfused red cells was not included.

Like the daily fluid intakes, the daily caloric intakes in the control group fluctuated widely, from 80 calories for the 3rd and 4th days of F. W. (Table III) to 2,200 calories for the 3rd and 5th days of R. B. (Table II). In fact, R. B. had almost the basic caloric requirements throughout his convalescence. The only one who approached this caloric intake in the control group. The nitrogen intakes varied still more widely, ranging from 0 for three days for F. W. (Table III), for four days for J. S. (Table IV), and for four days for D. R. (Table I, to 11.11 Gm. for the 6th day for R. B. (Table II), the averages being 3.31, 6.12, 5.5 and 3.97 Gm. for these four cases, respectively.

In the feeding group, except for the first day in the case of A. V. (Table V), and the first and second days in the case of F. R. (Table VI), in all the other postoperative days the intake was on the luxury level. The respect for the tradition of withholding feedings for the first few days postoperatively in abdominal cases, accounted for the "lean" first day for A. V., and first two days for F. R. In our last two cases, V. B. (Table VII), and P. F. (Table VIII), feeding was started after the first 12 hours, which period may still be shortened, with courage gained from further experience. Except for the three "lean" days mentioned above, the caloric intake in this group ranged from 3,050 to 4,700 (V. B.) daily. It may be mentioned that this latter amount was given in response to complaints of hunger on the part of a patient, who was being fed 3,360 calories a day—a phenomenon connected with convalescence which bears further investigation.

The nitrogen intake in the feeding group, except for the three "lean" days mentioned, ranged from 20.25 Gm. (A. V.) to 38.25 Gm. daily for the 5th, 6th and 7th days of P. F. The average daily intakes were 17.7, 23.22, 28.05 and 21.81 Gm., respectively, for the four feeding cases.

In the feeding group, the caloric and nitrogen values were mostly derived from amigen and nutramigen* in the feedings, although dextrose and amigen injections and blood transfusions contributed some part of the first days' intake. Amigen is a casein enzymatic digestate containing approximately 85 per cent amino-acids and 15 per cent polypeptides, each gram yielding 3.4 calories and 0.12 Gm. of nitrogen. Nutramigen contains, in addition to amigen, dextri-maltose, a neutral fat, arrowroot starch, calcium gluconate and brewer's yeast, and minerals added to simulate the quantities present in cow's milk. Nutramigen has been developed as a food for infants and is marketed as such. It yields 4.7 calories per gram and contains 2.7 per cent nitrogen. In preparing the feeding, the amigen and nutramigen were mixed

Both amigen and nutramigen were kindly supplied us by the Mead-Johnson Co,

with a convenient amount of physiologic saline or water to make the mixture easily instillable by means of a syringe through the feeding tube into the jejunum. The feedings were so spaced that from 50 to 150 cc. was given every hour. A larger amount might cause nausea and vomiting, either as a result of distention or of too rapid an absorption resulting in hyperaminoacidemia. The balance of the mixture was kept in the refrigerator, since it is a fertile medium for bacterial growth, and decomposition easily sets in.

Collection and Care of Specimens.—The 24-hour urine was preserved with thymol, measured, and kept on ice. In some cases in both groups, both urine and gastric suction specimens were sometimes pooled for two or three days and an aliquot part of the pooled specimens taken for nitrogen determination. In these instances the total nitrogen over the number of pooled days was recorded in the tables as one figure. The Wangensteen drainage (gastric suction) was preserved in sulfuric acid. Likewise preserved in sulfuric acid, were the stools collected and pooled over the study period. The discharges from the wounds were never large enough to be taken into consideration, random samples yielding negligible amounts of nitrogen.

The samples of blood for blood plasma protein determinations were taken in one of two ways. Where the specific gravity method of Barbour and Hamilton¹¹ was used, the anticoagulant used was heparin. Where a chemical method was used, the anticoagulant was sodium oxalate. The hematocrit was determined in the Sanford-Magath tube, and in most cases was read each time the plasma proteins were determined.

Chemical Methods.—As stated above, when the total plasma protein concentration only was needed, it was determined by the specific gravity method of Barbour-Hamilton,¹¹ using the apparatus designed by these authors. Where it was desired to obtain the albumin and globulin figures, the method of Wu and Ling as modified by Greenberg¹² was used.

In determining the nitrogen of the urine, stool and gastric drainage, the method of Rappoport as modified by Levy and Palmer¹³ was used.

ANALYSIS OF THE TABLES

The fluid, caloric and nitrogen and NaCl intakes have been discussed in a foregoing section of this paper.

Fluid Output. (Gastric Suction)—By this item is meant the amount of drainage, in cubic centimeters, yielded by the Wangensteen apparatus each 24 hours. The suction was kept up for from four to seven days. The amount in cubic centimeters varied from a minimum of 400 cc. (V. B.) to a maximum of 2,800 cc. (A. V.). As mentioned before, this source of fluid loss complicated the problem both of fluid and of sodium chloride replacement. The drainage of J. S. contained visible blood for the second and third days. The amount of nitrogen lost from this source will be discussed under the heading of "*Gastric Nitrogen.*" As a rule, the suction tube was left

in place for a shorter time in the control cases than in the feeding cases, in whom it was needed for feeding.

Urinary Output.—As might be expected from what has been said of the fluid intake, there was more fluctuation of the urinary volume in the control group than in the feeding group. Generally speaking, however, the urinary volume was quite adequate. The smallest output was 650 cc. for the first day of A. V., the first feeding case, when no provision was made for the gastric drainage. The fluctuations in the control group existed throughout the course of the convalescence, while in the feeding group the urinary volume was fairly well stabilized to from 1,000 to 1,900 cc. after the gastric suction was discontinued. The widest fluctuations were in the case of F. W., a control case, whose output ranged from a low of 700 cc. to a high of 3,550 cc. Incidentally, he also had a low blood plasma protein concentration of 5.23 Gm.% at the time of this excessively high output.

Urinary Nitrogen.—In the control group, except for R. B., the nitrogen excretion in the urine averaged respectively 13.69, 15.46, 18.03 and 11.74 Gm. daily. These figures are in the neighborhood of urinary nitrogen figures given for the ten days of complete starvation, as found in Succi, Cetti and Levanzin.¹⁴ They are, except for R. B., all above the 13 Gm. given as the nitrogen excretion of average persons. Brunschwig, *et al.*, gave figures for two cases of gastric resection, one, excreting 73.53 and the other 175.79 Gm. of nitrogen in ten days, averaging 7.35 and 17.58 Gm. respectively. Just how much of this excreted amount is "toxic loss," how much is starvation loss, as modified by previous undernutrition, is not clear.

In the feeding group, A. V. was taking an average of 17.78 Gm. of nitrogen and excreting an average of 11.21 Gm. daily; F. R. was taking in 23.22 and excreting 9.77 Gm. daily; V. B. was ingesting 28.04 and excreting 13.33 Gm., while P. F. was ingesting 35.63 and excreting 21.81 Gm. These figures suggest that A. V. and F. R. were ingesting perhaps less than they could fully utilize; that V. B. was perhaps getting the optimum amount, and that P. F. was perhaps ingesting an amount above the optimum. Both F. R. and V. B. had blood transfusion reactions, which no doubt accounted for the large amount of urinary nitrogen excreted during the days immediately following the transfusion. This would tend to introduce an error in the amount of nitrogen actually lost from the body.

Gastric Nitrogen.—This item represents the amount of nitrogen lost in the Wangenstein drainage. In the control group, the figures were, minimum .771 Gm. (D. R.), maximum 25.368 Gm. (J. S.), for any one day. The blood in the drainage of J. S. accounts for a part of this nitrogen. The average daily loss was 3.18, .815, .216 and 17.45 Gm. Aside from hemorrhage as a source of nitrogen loss, it is quite possible that the oozing of exudate from the operated viscus may also have contributed to this loss. In the feeding group, the average daily losses were higher, being 2.2, 5.33, 3.3 and 4.15 Gm., respectively, but how much, if any, of it represented refluxed feeding from the jejunum has not been ascertained.

Even taking the loss in the control group as the more nearly actual figure, it is clear that a considerable amount of nitrogen can be lost from this source.

Fecal Nitrogen.—The fecal nitrogen in both of these groups is low, with a tendency in the feeding group to be slightly higher. The only subject who almost approximated the classical average daily norm of 1.3 Gm. was V. B., in the feeding group, with an average of 1.25 Gm. of nitrogen excreted in the stools. In the control group, the lowest daily average was .21 Gm. (J. S.), and the highest 0.815 Gm. In the feeding group, the lowest daily average was 0.601 (A. V.) and the highest 1.26. These low figures are suggestive of the low fecal nitrogen excretion of Benedict's¹⁵ subjects under prolonged restricted feeding.

Total Nitrogen Output.—The daily total nitrogen output averaged 13.69, 16.4, 9.24 and 20.13 Gm. daily in the control group, and 12.33, 12.78, 17.3 and 15.38 Gm. in the feeding group. In the control group, therefore, the average total nitrogen loss of two cases is significantly higher than that found in complete starvation. The day-to-day output, however, fluctuated a great deal, and in three out of four control cases there were always some days when the output was considerably higher than that found in starvation.

The Nitrogen Balance and the Cumulative Nitrogen Status.—Except for the first day in the case of F. W., none of the four cases in the control group achieved nitrogen balance during any of the days under study; the nearest approximation to a balance was a loss of 0.61 Gm. of nitrogen on the part of F. W. on the 12th postoperative day. The average daily nitrogen losses were 10.37, 10.28, 3.73 and 16.4 Gm. daily. The sum-total of these losses were 114.09, 82.21, 44.8 and 141.11 Gm., respectively. This cumulative deficit is entered under the column entitled "Cumulative Nitrogen Status" in the tables.

In the feeding group, except for the three days of withholding feeding, positive balances were registered on all the days. The cumulative nitrogen surplus, after subtracting the deficit of the three "lean" days, were 38.25, 114.88, 130.95 and 123.56 Gm., respectively. This surplus is also entered under the heading of "Cumulative Nitrogen Status."

The Hematocrit and Plasma Protein Determinations.—In the absence of blood volume determinations and in the presence of multiple infusions, especially in the control group, these determinations have been robbed of much of their absolute value. Generally speaking, however, the tendency of the plasma protein level was downward in the control group, and upward or relatively stationary in the feeding group. This finding in the feeding group is more significant than the figures in the control group because of the better regulated fluid intake and the comparative absence of infusions. The sharp upswing of the total plasma proteins and hematocrit from 5.35 to 7.04 Gm.% in the case of F. W. is a bizarre phenomenon. Whether it is due to an hemoconcentration or to a rise of blood proteins, even while the body was still losing nitrogen, is only a matter of speculation.

In the case of the hematocrit values, the tendency of both groups is to

POSTOPERATIVE METABOLISM

dip below the preoperative figures, showing that in spite of the transfusions, there is some loss of blood. This is particularly true with those cases in which there have been blood transfusions reactions (F. R. and V. B.).

The Weight Curve and the Cumulative Nitrogen Status.—If a table is constructed by posting the cumulative nitrogen status during the period in one column, the equivalent of this in body tissue in a second column, and the gain or loss of body weight in a third column, a better picture of the relationship of these three factors may be seen. The equivalent of the nitrogen gain or loss in body tissues is arrived at by multiplying the result, deficit or surplus by the standard factor of 6.25, and multiplying the result, in turn, by five, assuming that the protein is deposited with 80 per cent water to form body tissues. Table IX represents this relationship in the eight cases studied.

TABLE IX			
Patients	Cumulative Nitrogen Status Gm.	Body Tissue Lost or Gained Gm.	Body Weight Lost or Gained Gm.
D. R.....	-114.09	-3455	-6950
R. B.....	- 82.21	-2569	-4300
F. W.....	- 44.8	-1397	-3430
J. S.....	-141.13	-4410	-5230
A. V.....	+ 38.24	+1195	+1540
F. R.....	+114.98	+3593	+3950
V. B.....	+130.95	+4092	+4710
P. F.....	+123.56	+3861	+4210

It will be seen from the table that while no linear relationship exists between the nitrogen deficit or surplus and body weight loss or gain, yet the trends are roughly parallel. Figures 1 and 2 represent this relationship graphically. Both the charts and the tables show that in the control group there was a significant loss of body weight, while in the feeding group there was a significant gain. Another interesting point in connection with body weight in the control group is that it required a fairly long time for the initial weight to be restored. Thus D. R. on discharge, 35 days postoperatively, was still 900 Gm. under the initial weight; R. B. almost reached his initial weight three weeks postoperatively; F. W. two weeks postoperatively was still 4,450 Gm. under his initial weight; and J. S. on the 17th postoperative days was 3,870 Gm. below her initial weight.

Of the two cases in the control group who were followed for 12 days, D. R. lost 115 Gm. of nitrogen and 6,950 Gm. of body weight, and F. W. lost only 45 Gm. of nitrogen and 3,430 Gm. of body weight. It is interesting to observe that two fasters—Succi (Florence, 1888), in 12 days of complete fasting lost 134 Gm. of nitrogen and some 7,700 Gm. of body weight, while Levanzin lost, in the same period, 120.53 Gm. of nitrogen and 6,760 Gm. of body weight. The weight losses of three other fasters for 12 days were—Jacques (1888) 6,970 Gm., Beatue (1907) 6,410 Gm. and Schenk¹⁴ (1906) 6,800 Gm. It is apparent that in spite of the infusions and transfusions given to the patients undergoing gastric resection, the nitrogen and body weight losses of some cases can approximate those of complete fasting.

Theoretically, the body weights of patients with hypoproteinemia may be higher than the actual weight, as a result of the loss in colloid osmotic pressure of blood proteins and the retention of water by the tissues (latent edema). In such a circumstance, the body weight would be sustained at a falsely high level, to undergo a sudden drop with restoration of colloid osmotic pressure to the blood. With D. R. there was no suggestion of this phenomenon taking place. With F. W., the only other patient with definite hypoproteinemia, the loss of only 260 Gm. of body weight in the first three days, in the face of a blood protein which fell from 6.3 to below 5.5 Gm. per cent, and the loss of 2,130 Gm. on the fourth day after the excretion of 3,550 cc. of urine on the previous day, is suggestive of this mechanism having been operative.

The Period of Hospitalization.—This study was not carried out with any planning, but was really an afterthought. A number of factors entered into determining when this period should be terminated, among them whether a patient has relatives at home to take care of him after his discharge. It is apparent that a patient living alone must stay in the hospital until he is stronger. In a future series, it is planned to have a better control of this factor. Meanwhile, the number of days of hospitalization of these two groups are interesting:

Control Group	Days
Name	
D. R.....	35
R. B.....	21
F. W.....	21
J. S.....	17
	<hr/>
Av.	23.5
Feeding Group	
A. V.....	22
F. R.....	17
V. B.....	14
P. F.....	14
	<hr/>
Av.	16.75 days

There is, thus, a shorter hospitalization period of 6.25 days in the feeding than in the control group.

Infusions and Transfusions: The number of infusions and transfusions administered to the patients in these two groups are shown in Table X.

TABLE-X

Control	No. of Days of Infusion	Total Infusions Given—L.	No. of Transfusions	Total Amount of Transfusions	
				Blood Cc.	Plasma Cc.
D. R.....	10	18	4	1,000 cc. W.B.*	1,000 cc.
R. B.....	7	19.5	6	1,500 cc.	1,050 cc.
F. W.....	2	7	1	500 cc.	
J. S.....	5	12	1	500 cc.	
Feeding					
A. V.....	2	3	1	500 cc.	
F. R.....	4	12	1	500 cc.	
V. B.....	1	4	0	0	
P. F.....	1	2	1	500 cc.	

*W. B. = Whole blood.

It will be seen that both the number of infusions and transfusions were markedly reduced in the feeding group. This was also the experience of Stengel and Ravdin,¹⁶ with their orojejunal feeding cases. In the last two patients, V. B. and P. F., the infusions were given in the first 12 postoperative hours, and V. B. had no transfusions, while the transfusion in P. F. as a result of the severe reaction seemed to have been more harmful than otherwise, reducing the hematocrit value significantly, and could well have been dispensed with. The greater comfort to the patient in the use of fewer infusions and the economic advantage of reducing the number of transfusions are considerable.

Postoperative Asthenia.—While the usual postoperative debility was present in the control group, it was interesting to note that it was minimal in the feeding group. This was most apparent in the last two feeding cases, V. B. and P. F., who got restless and asked to get up in a wheel chair on the eighth day. On the twelfth day they were helping move beds and weighing fellow patients. This absence of postoperative debility was also observed by Brunschwig, *et al.*, in one case, a patient who had gained 20.39 Gm. of nitrogen. Although this absence of asthenia seems to be definite in this series of four patients, it is still impressionistic. In a future series we propose to study this subject objectively.

Disadvantages of the Feeding Method.—The main disadvantage of this method of feeding is the discomfort caused by the presence of the nasal tube. This discomfort is relieved in 24 hours after the tube is removed. The other disadvantage is the objectionable taste of the mixture. When the mixture is administered through a tube, this difficulty is circumvented, but many patients rebel against taking it orally. If the patient is told that it is a "build-up medicine" which he will not have to take for more than a week (after the five to six days of tube feeding), however, he can usually be persuaded to "down" the mixture. Occasionally diarrhea occurs. Whether this is due to overfeeding or to other factors has not been determined.

In this series of four feeding cases, and in a large series of feeding with amigen and nutramigen to patients who were not under study, there was never any distention encountered.

DISCUSSION AND COMMENTS

The question arises, how does this attempt to maintain caloric and nitrogen equilibrium postoperatively differ from previous attempts? None of the technics employed in this study are essentially new. Various technics of postoperative tube feeding have been periodically reported. Elman and Brunschwig showed the feasibility of achieving nitrogen balance by parenteral feeding, and this has been repeated by Landesman and Weinstein.¹⁷

Stengel and Ravdin,¹⁶ in 1939, and Ravdin and Stengel,¹⁸ in 1940, reported an orojejunal method of feeding, using the Abbott tube, and an ingenious automatic feeding machine. Unfortunately, there was at that time no ready-made homogenous mixture available. Furthermore, no nitrogen balance

was done, and without knowing the gravity of nitrogen losses, no adequate replacement could be given, particularly as these authors emphasized only the necessity of a basal intake.

The first point of departure in this work from previous work is the utilization of the absorbing surface of the reaches of the intestines beyond the point of operative trauma for the absorption into the system of a feeding mixture which requires the minimum of digestive effort. The combination of the feeding tube and this mixture obviates the difficulties which bar the way to immediate postoperative feeding, especially in abdominal cases, namely, the vomiting, anorexia and impairment of the digestive processes caused by an operation. The second point of departure is the strict adherence to a caloric and nitrogen intake, which would at least fully replace the losses resulting from the operation.

To rely solely upon intravenous alimentation to do this is to put to heroic use a method which, at best, must remain an excellent adjuvant. Elman and Brunschwig both realize this, Elman saying: "The purpose of parenteral alimentation, in surgery at least, is to clear temporary hurdles"; and Brunschwig, *et al.*, stated: "Minimal caloric requirements, including sufficient protein (as amino-acids), may be met by intravenous nutrition." Thus, in order to give 1,749 calories, and a nitrogen intake of 18 Gm., Brunschwig gave as much as 4,500 cc. of fluid intravenously in six hours, an amount which must tax the circulatory system by the production of an acute plethora. And, unfortunately, the caloric and nitrogen requirements postoperatively are not often basal, as has been demonstrated by Cuthbertson,⁶ An analysis of the four cases reported by Brunschwig, *et al.*, as having registered a net gain of nitrogen ten days postoperatively, shows that only one achieved a positive nitrogen balance as a result of intravenous feeding. In Elman's report of 35 patients, in whom nitrogen balance was achieved by intravenous alimentation, only four postoperative cases were reported in detail, and in none of these four was a positive nitrogen balance consistently achieved. Recently, Gardner and Trent¹⁹ found similar difficulty in maintaining nitrogen balance by intravenous alimentation in patients with large nitrogen losses postoperatively. If to this limitation may be added the dangers of pyrogenic reactions, and of phlebitis and thrombosis of veins, the restoration of whose patency is never certain and which could be conserved for use in greater emergencies, the present tendency to rely mainly on intravenous infusions to supply caloric and nitrogen requirements seems unjustifiable.

Finally, two further points must be emphasized. The first is that blood and plasma transfusions, dramatic as they are in the restoration of the blood volume in acute hypovolemia caused by hemorrhage or acute loss of plasma proteins, cannot be depended upon as the sole caloric and nitrogen supply for the body. Sachar, Horvitz and Elman²⁰ are of the same opinion, and a little arithmetical calculation will show the strength of this statement. As shown above, the amount of plasma proteins in 500 cc. of transfused blood will yield

POSTOPERATIVE METABOLISM

70 calories and 2.8 Gm. of nitrogen. To supply the basic caloric requirement alone would require 26 transfusions a day! Were all the hemoglobin in the transfused blood also utilized for body energy, for which we have no evidence at present, only 55 Gm. of protein in the form of hemoglobin would

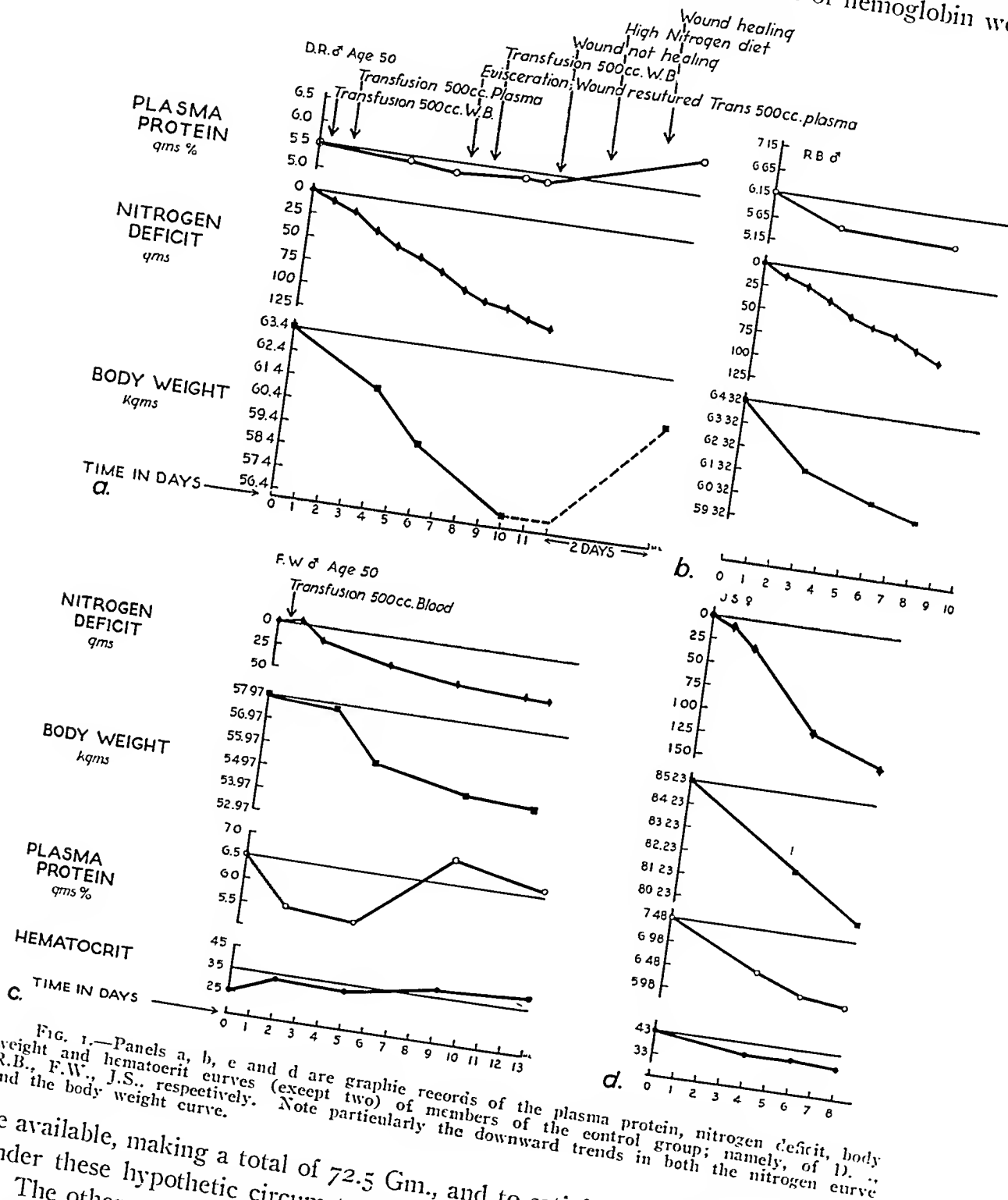


FIG. 1.—Panels a, b, c and d are graphic records of the plasma protein, nitrogen deficit, body weight and hematocrit curves (except two) of members of the control group; namely, of D., R.B., F.W., J.S., respectively. Note particularly the downward trends in both the nitrogen curve and the body weight curve.

be available, making a total of 72.5 Gm., and to satisfy the basal caloric needs under these hypothetical circumstances would require six transfusions a day. The other point, which Case D. R. suggests, is that unless provisions are made for full caloric and nitrogen maintenance postoperatively, patients

coming to operation with plasma protein concentrations near the "lower limit of normal" may be poor operative risks, for this so-called lower limit of normal already reflects some depletion of body proteins, which would be aggravated by the "toxic loss" of nitrogen and starvation incident to an

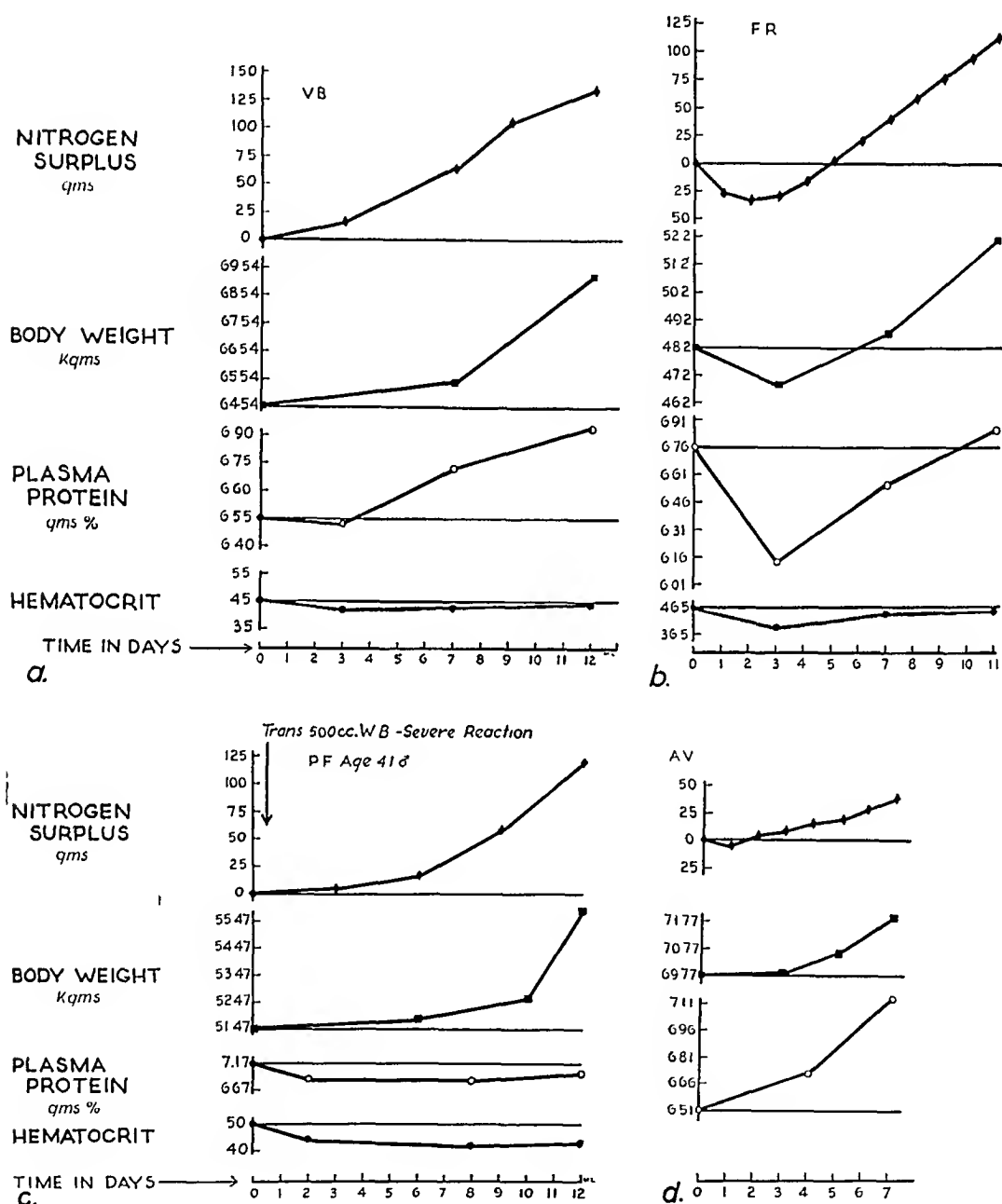


FIG. 2.—Panels a, b, c and d are graphic records of the nitrogen deficit, body weight, plasma protein and hematocrit (except one) curves of members of the feeding group, namely, of V.B., F.R., P.F., and A.V., respectively. Note the consistent upward trend in nitrogen surplus and body weight in all the four cases. The plasma protein curves are consistently upward in two and show a slight depression in two.

operation, leading to impaired wound healing. It may be safer for surgeons to set a higher "lower limit of normal" to surgical patients than is required in other specialties.

POSTOPERATIVE METABOLISM

It must be emphasized that these four cases are only preliminary, and point the way to a wider application of at least full caloric and nitrogen replacement in surgical patients. A number of refinements have still to be worked out, among them suitable feeding technics for different types of cases, and the optimum postoperative intake, and objective tests for strength and endurance.

SUMMARY AND CONCLUSIONS

(1) The nitrogen balance, the body weight and the plasma proteins of four patients with duodenal ulcer, and undergoing partial gastrectomy, and treated postoperatively by the standard ward routine, were followed for from 7 to 12 days. There was found to be in all these cases a cumulative nitrogen deficit, a progressive loss of body weight and a suggestive progressive fall of plasma protein concentration.

(2) In another group of four patients with similar pathology, and undergoing the same operation, in whom the caloric and nitrogen balance was maintained by tube feeding with an easily assimilable feeding mixture, there were achieved a positive nitrogen balance, a cumulative nitrogen surplus, and a progressive rise of body weight and of plasma proteins. There also seemed to be the minimum amount of postoperative asthenia.

(3) The technics employed in this study were discussed, as well as the fallacy of expecting to maintain nutrition by blood transfusions, and the necessity of a higher "lower limit of normal" of plasma proteins for surgical patients.

(4) The preliminary character of this work is emphasized.

The authors wish to acknowledge their grateful thanks to Dr. Victor Carabba who performed a number of these gastrectomies.

REFERENCES

- ¹ Jones, C. M., and Eaton, F. B.: Postoperative Nutritional Edema. *Arch. Surg.*, 27, 159, 1933.
- ² McCray, P. M., Jr., Barden, R. P., and Ravdin, I. S.: Nutritional Edema Effect on Gastric Emptying Time before and after Gastric Operations. *Surgery*, 1, 53, 1937.
- ³ Thompson, W., Ravdin, I. S., and Frank, I. L.: Effect of Hypoproteinemia on Wound Disruption. *Arch. Surg.*, 36, 500, 1938.
- ⁴ Koster, H., and Shapiro, A.: Serum Proteins and Wound Healing. *Arch. Surg.*, 41, 723, 1940.
- ⁵ Hartzell, J., Winfield, J. S., and Irvin, J. L.: Plasma Vitamin C and Serum Protein Levels in Wound Disruption. *J. A. M. A.*, 116, 669, 1941.
- ⁶ Cutlbertson, D. P.: Postshock Metabolic Response. *Lancet*, 1, 433, 1942.
- ⁷ Elman, R.: Parenteral Replacement of Protein with Amino-Acid of Hydrolyzed Casein. *ANNALS OF SURGERY*, 112, 594, 1940.
- ⁸ Brunschwig, A., Clark, D. E., and Corbin, N.: Postoperative Nitrogen Loss and Studies on Parenteral Nitrogen Nutrition by Means of Casein Digest. *ANNALS OF SURGERY*, 115, 1091, 1942.
- ⁹ Riggs, H. E., Reinhold, J. G., Boles, R. S., and Shore, P. S.: Qualitative Circulatory Deficiencies Observed in Peptic Ulcer: Chemical Composition of the Blood. *Am. Jour. Dig. Diseases*, 8, 383, 1941.

- ¹⁰ Coller, F. A., and Maddock, W. G.: Electrolyte Balance. *Surg., Gynec. & Obst.*, **70**, 340-354, 1940.
- ¹¹ Barbour, H. G., and Hamilton, W. F.: The Falling-Drop Method for Determining Specific Gravity. *Jour. Biol. Chem.*, **69**, 625, 1926.
- ¹² Greenberg, D. M.: The Colorimetric Determination of the Serum Proteins. *Journ. Biol. Chem.*, **82**, 545, 1929.
- ¹³ Levy, M., and Palmer, A. H.: Iodometric Estimation of Small Quantities of Nitrogen with Distillation. *Jour. Biol. Chem.*, **136**, 57, 1940.
- ¹⁴ Benedict, F. G.: A Study of Prolonged Fasting. Carnegie Institution of Washington, Publication, No. 203, pp. 73 and 251, 1915.
- ¹⁵ Benedict, F. G., Miles, W. R., Roth, P., and Smith, H. M.: Human Vitality and Efficiency under Prolonged Restricted Diet. Carnegie Institution of Washington, Publication No. 280, 1919.
- ¹⁶ Stengel, A., Jr., and Ravdin, I. S.: Maintenance of Nutrition in Surgical Patients with a Description of Orojejunal Method of Feeding. *Surgery*, **61**, 511, 1939.
- ¹⁷ Landesman R., and Weinstein, V. A.: The Intravenous Use of Amino-Acids for Nutritional Purposes in the Surgical Patient. *Surg., Gynec. & Obst.*, **76**, 300, 1942.
- ¹⁸ Ravdin, I. S., Stengel, A., and Prushankin, M.: Control of Hypoproteinemia in Surgical Patients. *J. A. M. A.*, **114**, 107, 1940.
- ¹⁹ Gardner, C. E., and Trent, J. C.: Intravenous Amino Acid Administration in Surgical Patients using an Enzymatic Casein Digest. *Surg., Gynec. & Obst.*, **75**, 657, 1942.
- ²⁰ Sachar, L. A., Horvitz, A., and Elman, R.: Studies on Hypoalbuminemia Produced by Protein-Deficient Diets. *J. Exp. Med.*, **75**, 453, 1942.

PREOPERATIVE SCRUBBING IN ABDOMINAL SURGERY

I—EXPERIMENTAL STUDIES*

J. K. BERMAN, M.D., ALAN D. HOUSER, M.D.,

AND

WILLIAM A. KURTZ, M.D.

INDIANAPOLIS, INDIANA

FROM THE DEPARTMENT OF SURGERY, INDIANA UNIVERSITY SCHOOL OF MEDICINE, AND THE SURGICAL SERVICES OF THE ROBERT W. LONG AND JAMES WHITCOMB RILEY HOSPITALS, INDIANAPOLIS, IND.

ABOUT 35 YEARS AGO Theodore Kocher¹ emphasized the value of preoperative scrubbing in the preparation of a patient for surgical operation. In his text book of Operative Surgery he makes the following statements: "It is remarkable how many people of the present day refuse to be convinced that dirt can be really and readily removed by means of simple running water. It is no uncommon sight to see the surgeon and his assistants scrupulously careful about the cleansing and scrubbing of their own hands, while the patient's skin is washed with a little soap and lotion immediately before the operation, receiving subsequently a few doses of corrosive lotion, proceedings which imply a contradiction.

"There is no reason why every patient should not have the benefit of a vigorous cleansing (soap and water) from head to foot in the surgical sense of the term. This washing, which is carried out in a warm bathroom the day before operation, should be preferred to the practice of some surgeons who apply antiseptic poultices to the skin at the site of the operation." Many surgeons still follow Kocher's advice.

It is difficult to prove clinically whether or not preoperative scrubbing is effective. However, in the experimental animal this can be ascertained more accurately. At the outset, we should define our terms, and by scrubbing we mean the use of a small, soft hand brush with soap and unsterilized warm water applied to the part vigorously for about eight minutes. The term 'preoperatively' is used to include a period up to 12 hours before operation. Immediate surgical sterilization is not included in this study.

In order to determine the efficacy of scrubbing, we decided to test the method on guinea-pigs and dogs. At the same time, a group of patients were treated by scrubbing, in an effort to evaluate the method clinically. These results are to be reported in a supplementary paper.

EXPERIMENTAL STUDIES

First, we wanted to establish normal standards so that variations could be charted. Daily leukocyte counts and rectal temperatures were recorded in 15 guinea-pigs. Our conclusions were that leukocyte counts and body temperatures are not stable in guinea-pigs, varying with room temperature

* Aided by a grant from the Eli Lilly Research Fund.

and other factors not determined. These reactions are also not reliable guides in evaluating the general condition of an animal with normally healing or with infected wounds. There is, however, one significant finding in scrubbed guinea-pigs which is only rarely observed in the controls. This is an increase in the number of leukocytes, averaging about 7000 per cu. mm. immediately after operation (Chart 1): Although some animals die of

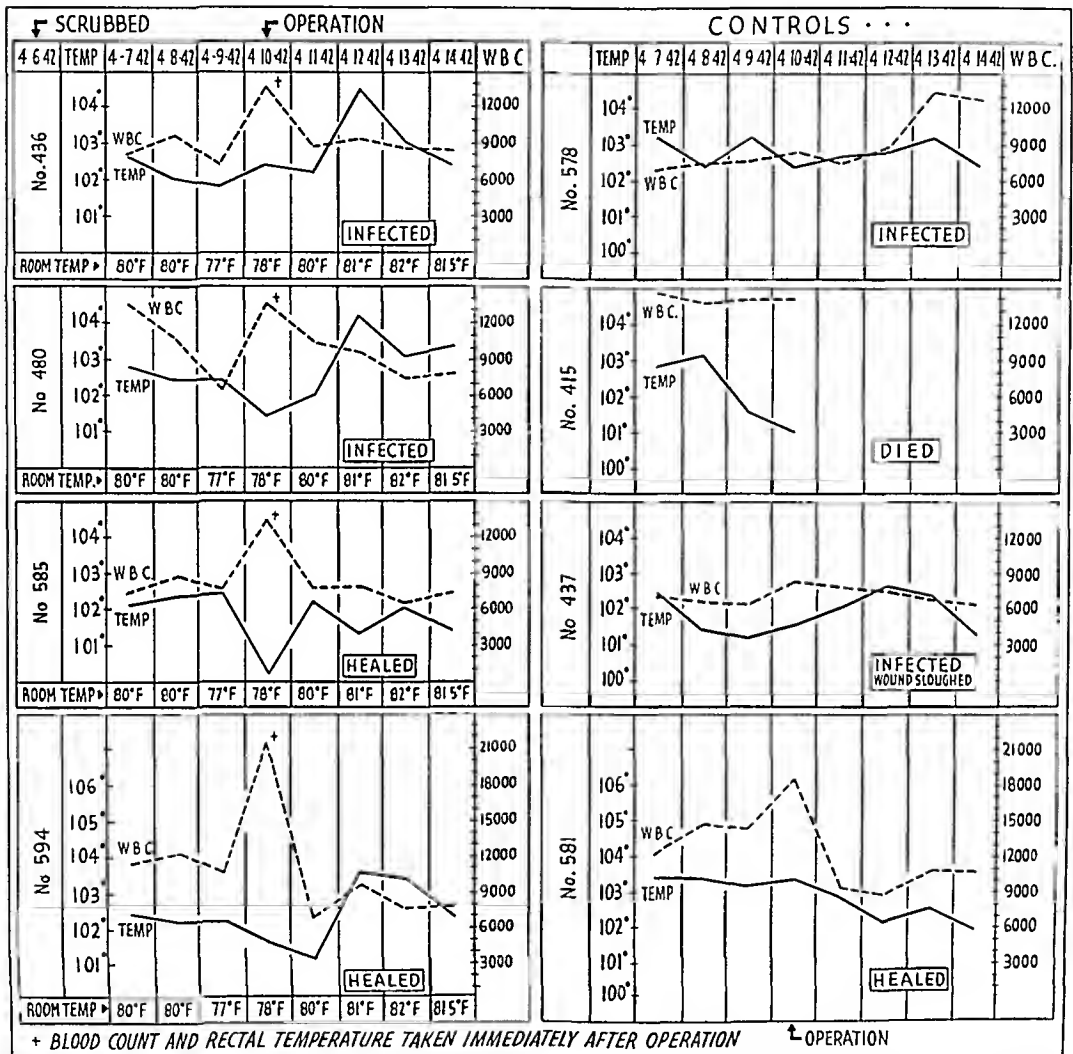


CHART 1.—Charts showing room temperature, body temperature and leukocyte counts in four guinea-pigs which had been scrubbed 96 hours prior to operation and four controls. Three-tenths of a cubic centimeter of a pure culture of *Staphylococcus aureus* was introduced into the abdominal wound at the time of operation. Note the increase in leukocytes immediately after operation in the scrubbed pigs.

staphylococcic septicemia after inoculation, showing leukocyte counts of 500 or less, there was usually a leukocytosis, and the body temperatures remained high. In environmental temperatures of 70° to 80° F. infected guinea-pigs were found to have temperature, ranging up to 106° F.

NORMAL RATE OF HEALING

The abdominal wall of guinea-pigs was shaved, cleaned with soap and water, and antiseptized with ether and tincture of methiolate. Aseptic

SURGICAL SCRUBBING

technic was used, and operations were performed under ether anesthesia. An incision five centimeters long was made in the abdominal wall, extending through the skin, subcutaneous tissue and abdominal muscles. The peritoneum was not opened. Incisions were closed with interrupted silk sutures in the muscle layers, subcutaneous tissue and skin. In the first group of pigs, bandages were applied and the legs fastened with rubber bands, as suggested by Du Mortier.² However, this was found to be impractical, as the pigs developed edema of the legs and back and if not restrained they tore the dressings off. We, therefore, decided to observe the normal healing without dressings. The pigs were accordingly returned to their clean cages immediately after operation. Fourteen pigs were studied. Eleven wounds healed *per primam*. Three of this group, or 21.4 per cent, developed infections in the wound. The word 'infection,' as used here, implies any evidence of bacterial action in the tissues, either grossly or microscopically. On gross examination, none of these wounds were thought to be infected for there were no clinical signs to indicate this. Microscopically, some of them did show evidence of infection.

This study, which was repeated three times, with similar results, revealed that abdominal wounds in guinea-pigs usually heal without infection when made under the aseptic technic described, even though dressings are not applied. Since some of the animals were operated upon during the summer and some in the winter, the effect of high and moderate temperatures on wounds could be observed. It was found that wounds heal in 4-6 days (average 5+ days) in moderate room temperature (70°-80° F.). In high external temperatures (100°-110° F.) wounds required 7-13 days (average 9+ days) for healing.³ Low temperatures were not tried. This observation may be important in the present crises, for our forces are stationed in parts of the world where temperatures vary greatly. Since the body temperature of the pig is elevated proportionately to room temperature, we may deduce that high body temperatures retard, but do not prevent healing.

REACTION OF FRESH WOUNDS TO CONTAMINATION BY STAPHYLOCOCCUS AUREUS

Having determined the normal reactions of guinea-pigs to incisions made under aseptic technic, we next wished to learn the effect on the wound when a pure culture of *Staphylococcus aureus* was introduced. Such a culture was obtained from a patient with a carbuncle. The organism was grown six hours upon chopped meat medium, transferred every 24 hours, and occasionally plated on blood agar to check for purity. Virulence of the organism was determined by injecting the culture subcutaneously into guinea-pigs. The smallest dose which uniformly produced an abscess without causing death of the animal, when a six-hour culture was used, was found to be 0.3 cc. Abscesses were checked by microscopic examination. Virulence was maintained with surprising uniformity. Before every group of experiments the organism was injected into guinea-pigs and then reisolated from the resulting abscesses. Direct inoculation of the fresh wound was made by placing 0.3 cc.

of the six-hour culture of *Staphylococcus aureus* into the incised abdominal muscles. Incisions and closures were performed exactly as in the controls. Sixty-seven and one-half per cent of the animals developed infections in their wounds.

Many experiments were now undertaken in an effort to repeat the findings of Du Mortier,² who demonstrated the high degree of immunity which develops in granulation tissue. Also, studies were made to determine the extent of the local immunity by making multiple incisions at various sites in the abdominal wall at different times. By this method we were able to prove that the immunity in a wound does not extend beyond the area of granulation tissue. These experiments will be published subsequently.

THE EFFECT OF SCRUBBING UPON THE PRODUCTION OF WOUND IMMUNITY

The body reacts locally by inflammation and exudation whether the injury is produced by mechanical, bacterial, chemical, or any other trauma. We thought that perhaps scrubbing the abdomen might be a factor in the production of immunity. Thirty-four guinea-pigs were studied. They were anesthetized with ether, and their abdomens were shaved and then scrubbed with a hand brush such as is used by surgeons in the scrub room. This was done for five to eight minutes depending upon the reaction of the skin. Care was taken not to bruise or injure the abdominal wall. At the end of 24, 48, 72, 96, 120, and 144 hours after scrubbing, an incision was made in the abdominal wall under aseptic technic, exactly as previously described, and 0.3 cc. of a culture of *Staphylococcus aureus* was introduced. The experiment was then repeated, scrubbing the abdominal wall on six successive days. On the 6th day, all pigs were operated upon and the culture introduced as previously described. Four controls were operated upon without scrubbing in each series.

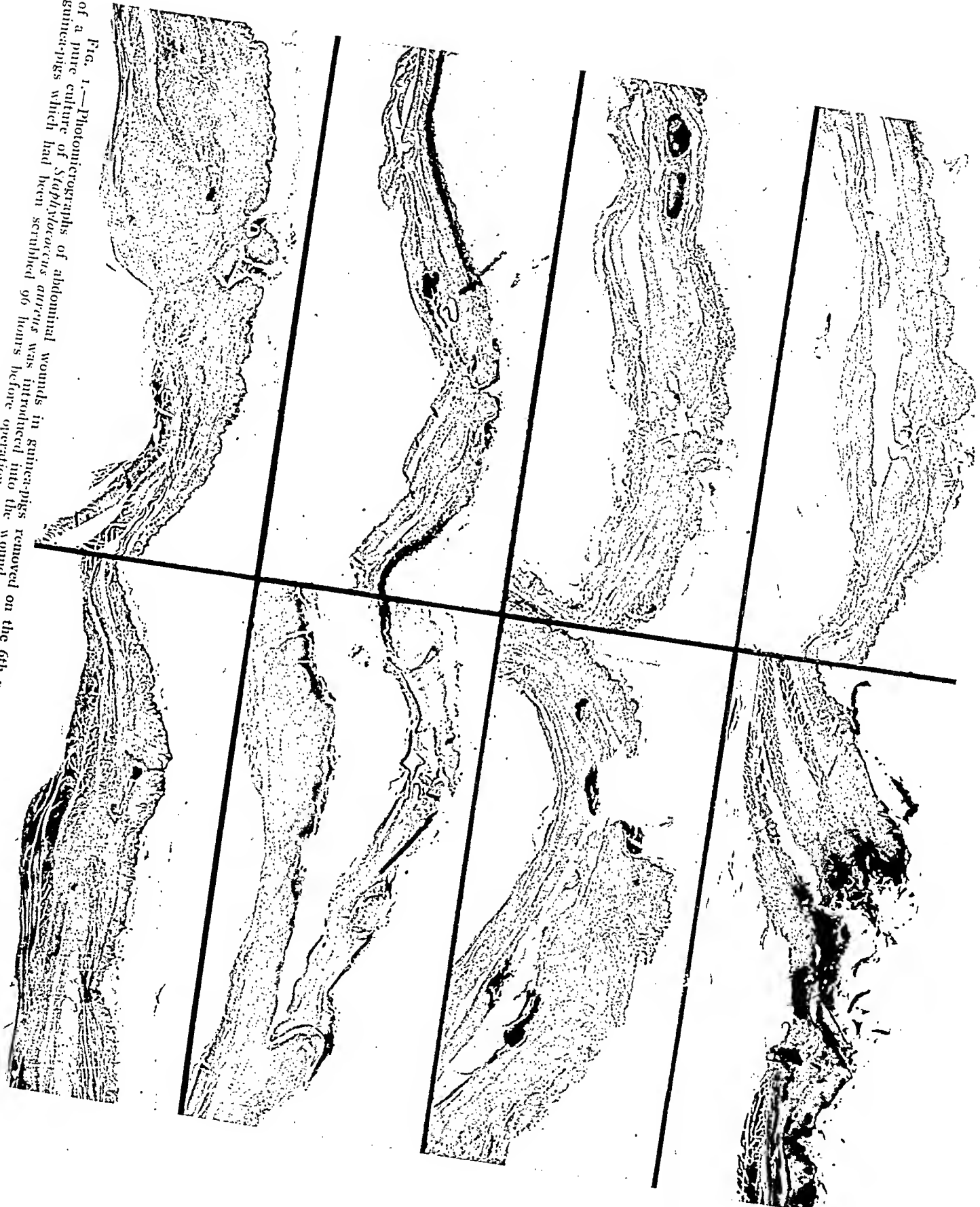
Seventy-five per cent of the guinea-pigs scrubbed 24, 48 and 72 hours before operation were infected. Fifty per cent of the guinea-pigs scrubbed 96 and 120 hours became infected. Sixty-seven and one-half per cent of the controls were infected.

In all instances the wound bled much more freely in the scrubbed pigs than in the controls. Grossly, the scrubbed pigs seemed to have infection in only 20 per cent. On the 6th postoperative day sections were taken from the abdominal wounds. Examination of these sections microscopically failed to reveal any consistent discernible difference in the degrees of infection in the scrubbed and unscrubbed pigs (Fig. 1). When the experiments were repeated the difference again was not in individual wounds but in the per cent of animals infected.

In order to check our findings, four guinea-pigs were prepared in the manner described above. Instead of using a six-hour culture we used a 24-hour culture of *Staphylococcus aureus*, and instead of 0.3 cc. we used 0.5 cc. in the incision. A second group of eight pigs was scrubbed 96 hours previous to operation, using the same culture. One of the controls died within 24

SURGICAL SCRUBBING

Fig. 1.—Photomicrographs of abdominal wounds in guinea-pigs removed on the 6th postoperative day. Three-tenths of a cubic centimeter of a pure culture of *Staphylococcus aureus* was introduced into the wound, as described in the text. The sections on the left are from guinea-pigs which had been scrubbed 96 hours before operation. On the right are controls. (x 4.5—Hematoxylin and eosin)



hours of a staphylococcus septicemia. Another died on the 4th postoperative day with a large abdominal abscess. The remaining controls survived but developed wound infections. All of the animals which had been scrubbed 96 hours previously showed infections in their wounds (Fig. 2). It is apparent from this study that the size of the dose plays an important rôle in the resulting infections.

EFFECT OF SCRUBBING THE ABDOMEN UPON PERITONEAL IMMUNITY

A group of eight guinea-pigs was now studied for intraperitoneal immunity. All operations were performed as previously described except that the peritoneum was opened. Three-tenths of a cubic centimeter of a pure culture of *Staphylococcus aureus* was introduced and the abdomen closed with interrupted silk sutures in layers. Five of the animals developed wound infections. All recovered. At autopsy, none showed any evidence of peritonitis.

Another group of eight pigs was studied in a similar manner except that foreign bodies, such as 18-inch knotted strands of sterile silk suture, were introduced in the peritoneal cavity. By this technic it was possible to produce a small abscess about the suture which was entirely localized by the omentum and adhesions when the animals were autopsied. Four of the abdominal wounds became infected although the culture was introduced into the abdomen with a glass pipette. One pig died of peritonitis and wound infection.

The same experiment was repeated with preoperative scrubbing. There was no difference in the intraperitoneal reaction from the control. However, only about 50 per cent of the pigs scrubbed 96 hours before operation developed wound infections.

SCRUBBING EXPERIMENTS UPON DOGS

In an effort to further study the problem we decided to perform similar experiments upon dogs. Eight healthy animals were anesthetized with ether, the abdomen was clipped, shaved and scrubbed for eight minutes, then prepared with ether and tincture of methiolate. A longitudinal paramedian incision 10.5 cm. long was made through the skin, subcutaneous tissue and anterior sheath of the rectus muscle. The rectus muscle fibers were separated. Three cubic centimeters of a six-hour culture of *Staphylococcus aureus* was introduced posterior to the muscle, then the rectus muscle and anterior sheath were closed using interrupted silk sutures. The skin was sutured with the same material. A second group of eight dogs was scrubbed for eight minutes, 96, 72, 48 and 24 hours before operation and the experiment was repeated.

These experiments simply corroborated previous observations except that only 50 per cent of the controls were infected when male dogs were used. The female dogs invariably developed an extensive infection which involved breast tissue, showing severe mastitis. Fifty per cent of all scrubbed dogs, regardless of time up to 120 hours, showed wound infections. There

SURGICAL SCRUBBING

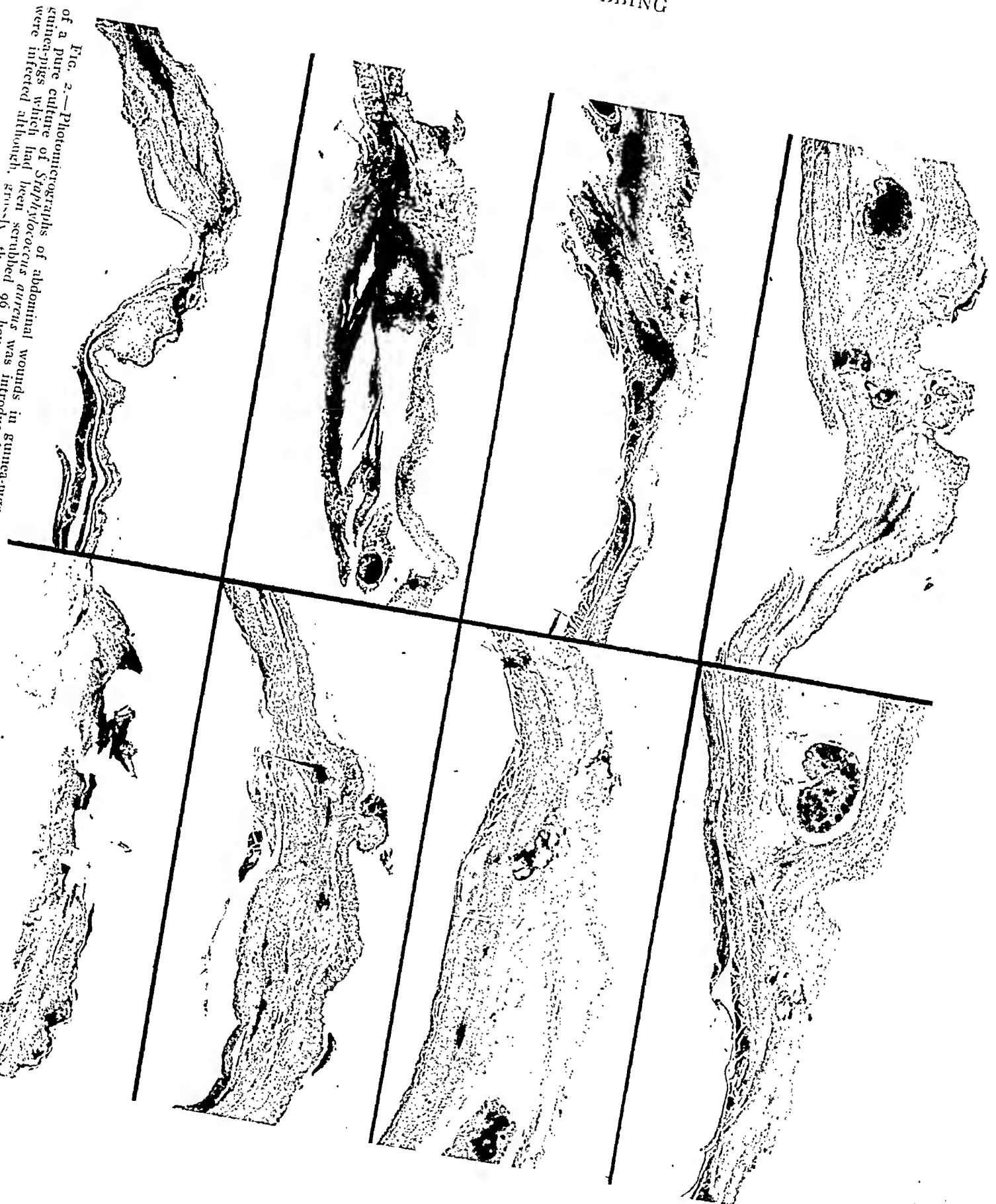


Fig. 2.—Photomicrographs of abdominal wounds in guinea-pigs removed on the 6th postoperative day. Five-tenths of a cubic centimeter of a pure culture of *Staphylococcus aureus* was introduced into the wounds, as described in the text. Sections on the right were taken from controls. (X 4.5—Iodoxylin and cosin)

were infected although, *crossly*, there was more swelling, drainage and tendency to slough in the controls. Sections on the left were taken from controls. (X 4.5—Iodoxylin and cosin)

was one death in a female dog with extensive mastitis and staphylococcus septicemia.

Twelve more dogs were operated upon, repeating the above experiment, with a study of daily temperatures and blood counts. Four animals were used as controls. The other eight were scrubbed 96, 72, 48 and 24 hours before operation. It was found that the temperature and blood counts were not reliable guides as to the presence or absence of infection. In Dog No. 231 leukocytes numbered 20,000 and 21,000 daily for four days, and yet the wound remained clean, whereas in Dog No. 233 the leukocyte count was 13,000, 11,000 and 8,000, yet his wound was grossly infected. This observation fits in fairly well with that observed clinically, for patients do not as a rule run a high temperature or leukocytosis with superficial wound infections. This is probably due to the fact that the antigen is not retained under pressure, due to looseness of tissue or early drainage. When the eight dogs that had been scrubbed were compared with the normal controls, it was impossible to determine which had had the previous scrubbing. About one-half of the animals were infected in each group.

Another study upon the effects of scrubbing in dogs was made as follows: Four animals were selected as controls and four were prepared by scrubbing 48, 24 and 12 hours before surgery. In addition, two dogs were scrubbed 96 hours before surgery and then again 24 hours before operation. In this group the 10.5 cm. incisions extended only to the anterior sheath of the rectus muscle. Also, the amount of culture introduced was calculated according to the body weight of the animal, based on the smallest amount that regularly produced wound infections without death. This was one cubic centimeter of culture for each 4.5 kilograms of body weight. Blood counts and daily temperatures were recorded. As in previous experiments it was impossible to identify those dogs that had been scrubbed from the normal controls, either grossly or microscopically. We may conclude from these experiments that the size of the dose had little to do with the resulting infections.

DISCUSSION

Since the antigen employed in our experiments was standard, infection could only occur as a result of change in the resistance of the inoculated animals. Scrubbing the abdominal wall for five to eight minutes with soap and water apparently does not greatly alter the resistance of animals to standard doses of staphylococci. However, it should be noted that guinea-pigs scrubbed 24 hours before operation showed a higher percentage of infection than did controls. Perhaps, this is due to a lowered resistance which may last 24 hours or longer after trauma. It is also significant that in guinea-pigs the incidence of infection was less in those which had been scrubbed four or five days before operation. This may be due to the development of increased local tissue resistance from the trauma of scrubbing following the lag-period described by Du Mortier, or the increase in leuko-

SURGICAL SCRUBBING

cytes may be a factor.² Grossly, the difference was striking, and we thought that this method of scrubbing protected 80 per cent of the animals against infection. This observation was not borne out by microscopic examination of the wounds. Many surgical wounds are described as clean in patients, which on microscopic examination would no doubt reveal subclinical infections as commonly as observed in the experimental animal.

Clinically, there is often an increased amount of wound bleeding in abdominal incisions made in the presence of active intraperitoneal infection. We sought to reverse this phenomenon and see its effect upon intraperitoneal immunity. No demonstrable reaction or increase in resistance to intraperitoneal contamination could be demonstrated by abdominal scrubbing.

It must be admitted that the scrubbing as ordinarily practiced clinically is merely a cleansing process and is in no way comparable to the surgical scrubbing of our experimental animals. In order to test the efficacy of this method of surgical preparation we selected a group of patients with intestinal fistulae, for in this group there was obvious contamination of the abdominal wall. These cases will be published in a supplementary report.

CONCLUSIONS

1. The body temperature and leukocyte counts in experimental animals with surgical wound infections are not reliable guides for the detection of such infections.
2. High environmental temperatures in experimental animals retard wound healing.
3. Surgical scrubbing of the abdominal wall with soap and water 24, 48 and 72 hours before operation does not protect animals against wound infection. It may predispose to a decreased resistance.
4. Scrubbing 96-120 hours before surgery seems to increase resistance slightly in guinea-pigs, probably due to the stimulation of the blood supply. There is a significant increase in the number of leukocytes immediately after surgery in this group.
5. In dogs, resistance to infection was not influenced by preoperative scrubbing, regardless of the time interval before operation or of the dose of *Staphylococcus aureus* used.
6. Scrubbing the abdominal wall does not affect the peritoneal resistance.

The authors wish to gratefully acknowledge the assistance of Dr. Lyle Weed, of the Department of Bacteriology, Indiana University School of Medicine.

REFERENCES

- ¹ Kocher, Theodore: Operative Surgery. The Macmillan Co., New York, 1911.
- ² Du Mortier, Jean Jacques: The Resistance of Healing Wounds to Infection. Surg. Gynec. and Obst., 56, 762-766, April, 1933.
- ³ Brooks, B., and Duncan, G.: Influence of Temperature on Wounds. ANNALS OF SURGERY, 114, 1069, December, 1941.

SYMPOSIUM ON PROBLEMS RELATING TO LAW AND SURGERY

THE LATE EFFECTS OF CRANIOCEREBRAL INJURIES

A CONSIDERATION OF THE CRITERIA NECESSARY
TO EVALUATE THE POSSIBLE CAUSES

DONALD MUNRO, M.D.

BOSTON, MASS.

FROM THE DEPARTMENT OF NEUROSURGERY, BOSTON CITY HOSPITAL, BOSTON, MASS.

PRACTICALLY every member of the medical profession and many lawyers have had occasion from time to time to try to estimate the significance of symptoms which were the subject of complaint by the patient or client and which were allegedly caused by an antecedent blow on the head months or years previously. The difficulty and confusion that arise when attempts are made to separate the symptoms and signs that are traceable to organic as opposed to so-called functional changes is, and has been, generally recognized. This confusion is rendered more chaotic by the tendency on the part of the medical and legal professions to be careless, or grossly inaccurate, in making and accepting the original diagnosis and in estimating therapy and prognosis in terms of pathology. This is enhanced by the public's indifference to the need for such accuracy. Such examples as the almost universal use of the term "concussion" to cover all varieties of craniocerebral injuries; and the unjustified importance granted by the legal profession to the visible "fracture of the skull," which is of no significance, in comparison with the neglect of the invisible brain injury which is actually the cause of all the symptoms, are all too common. An equally usual but no less troublesome factor is the ease with which any physician who is legally entitled to practice medicine in this Commonwealth can qualify himself in our courts as an expert in a subject about which he actually knows little or nothing and in which his experience will hardly compare favorably with that of a well-trained house-officer. Because of this, the court is forced to resort to the legal subterfuge of considering the significance of such testimony in the light of the "weight of the evidence." This imposes on the judge, commissioner or jury the duty of interpreting the medical significance of the facts as presented to them in terms of the witnesses' personality, his ability to speak extemporaneously and his salesmanship instead of on the basis of his professional qualifications. It is evident that the solution of this problem is not to be taken lightly, and must await education in the need for accuracy of expression and thought when dealing with such an important medicolegal matter as injuries of the nervous system.

I have had occasion to point out the late effects exerted by the proper approach by both the doctor and the patient to the latter's convalescence.¹

CRANIOCEREBRAL INJURIES

Denny-Brown,² Symonds,³ and Jefferson, Cairns and Brain⁴ have studied the end-results of craniocerebral injuries among a certain group of casualties in the British Army. Cairns,⁵ Symonds,⁶ the author, and many others, have written on various aspects of the surgical and early diagnostic phases of craniocerebral injuries. Much of this work is not germane to the present discussion however. That by Denny-Brown,² and Symonds³ is the most pertinent but because their conclusions are drawn from a study of British Army casualties, and comprise a special group of men living and treated medically under special conditions, who are all possessed of a common language and a great emotional urge to return to their original jobs if at all possible, their conclusions may not apply at all in the study of a group of injured drawn by-and-large from American wage-earners, and, in any event, should not be considered usable without further confirmation. The standards of living and the efficiency of medical care in these latter are as varied as their different languages and customs. If such patients have any emotional urge to return to their former jobs it is in spite of the influence of their friends, families and lawyers, and is influenced, moreover, by the effect on their morale of getting something—that is compensation—for nothing, which is the privilege of not working for as long as they can produce sufficiently disabling symptoms.

This is perhaps an oversimplification of an extraordinarily complex question as far as estimating the genuineness of the patient's symptoms is concerned. The impact of even a minor craniocerebral injury on the personality of a workman who is constitutionally unable to hold a job or who is so emotionally unstable that his family life is continually disrupted, will be decidedly different from that of the same injury on the personality of an emotionally stable, intellectually competent, adequate individual. If this comparison is carried either to the extreme of no injury plus a psychotic or psychopathic personality, or of a maximum injury to a completely normal personality, and the other possible combinations and their effects and interplay imagined, the importance and magnitude of this one aspect of this problem becomes immediately evident. If to this are added the varying influences exerted by the accuracy of diagnosis, the efficiency of treatment, the potentiality for harm that lies in an uneducated public opinion, in insurance adjusters, lawyers, friends, members of the family and other interested advisors; the amount and severity of any permanent residual loss of function; the influence of recognized or unrecognized intercurrent diseases, advancing age, intentional or unintentional malingering, impairment of judgment, and the like, on the part of the patient, some slight conception of the need for clarification of this matter can be had.

As far as I know, there are no reliable or worth while data on the effect of the relationship between a craniocerebral injury and the pretraumatic personality of the injured. This phase of the larger problem must await further and more detailed study of patients in both the acute and late.

stages of their injuries. No attempt will be made to deal with it here. I do however, feel that there are available certain other data relative to the diagnostic criteria that must and can be met if the symptoms alleged to have been originally caused by an antecedent craniocerebral injury are to be properly evaluated, a diagnosis made and therapy recommended at a late date. These criteria are tentative and will doubtless be modified many times as experience with them accumulates. The chief justification for bringing them to the attention of the medical and legal professions is that at least a start will have been made toward the solution of this vexing matter. They are based upon experience extending over a number of years, and are exemplified here by statistics drawn from a group of 50 patients injured in industry and seen and studied by myself during the past 18 months as an impartial examiner for the Massachusetts Industrial Accident Board. Such a small series justifies only the grossest statistical conclusions, but until many hundreds of such patients have been studied and tabulated there is reason to believe that it is as accurate as a somewhat larger but still inadequate series would be. It has the additional advantage of unity, in that all are workman's compensation cases, and of impartiality, in that the data have neither been collected in the interest of the complainant nor of the respondent.

This series includes 8 female and 42 male patients. The age was known in 39 of the 50 (32 males and 7 females). The oldest patient was 71 and the youngest 18, both being males. Similar figures for the women were 44 and 19, respectively. The interval between the date of the injury and the time of the first examination was known in 49 instances. This was considered in relation to the diagnosis as determined at this examination. The diagnostic classifications, which are discussed in more detail below, were divided under five headings: *Organic*, in which the cause of the symptoms was believed to be organic and certainly related directly to the alleged accident; *posttraumatic-state*, in which the cause of the symptoms was believed to lie in the nonorganic spheres and to be not necessarily directly related to the alleged accident; *intercurrent disease* and *no disease*, in the first of which the cause of the symptoms was believed to lie in an intercurrent disease having no relationship to the alleged accident, and, in the second of which, the symptoms and signs were of such character that it was believed that there was no disease of any kind present at the time of the examination; and, finally, *double diagnosis* in which two diseased conditions were believed to be simultaneously present. The average interval between the receipt of the injury and the first of my examinations in the organic group, was 14.5 months; in the posttraumatic-state group 12.5 months; in the double diagnosis group 13 months; in the intercurrent disease group 14.25 months, and in the no disease group 8 months. The longest intervals were 31 months in the organic and 30 months in the posttraumatic groups. The shortest intervals were 2 months in each of the same two groups.

CRANIOCEREBRAL INJURIES

There were 15 patients in the organic, 18 in the posttraumatic-state, 6 in both the no disease and intercurrent disease, and 4 in the other group. Seven patients were examined a second time, and in 1 patient the classification could not be determined. This patient reported for examination 10.5 years after the injury that was alleged to have caused his symptoms. No data were collected in regard to the marital state or the kind of work that was being done at the time the alleged injury is said to have occurred. I do not believe that, with the possible exception of a tendency on the part of the patients classed in the no disease group to report, on the average, twice as quickly for examination after they have recovered from their acute episode as those in the other groups, these data have any diagnostic or prognostic significance. Even the exception noted cannot be taken too seriously because the time when the examination was performed was conditioned by such factors as the diligence of the patient's lawyer, the resistance of the insurer's counsel and the state of the docket of the Industrial Accident Board. These data are included only because if they were not it would inevitably be suggested that their omission was significant.

VERIFICATION OF THE INJURY

The criteria sufficient to justify a conclusion that the symptoms and signs complained of by the patient at a late date after an antecedent accident are both positive and negative and action based on such conclusions—whether therapeutic or legal—are weakened by just that much if and when either class is not investigated. Among the fundamental information that must be obtained in every case before anything further can be decided is whether the patient has actually sustained a blow on the head, and, if so, whether there is reason to believe it was sufficiently severe to produce resultant changes in the brain, and, finally, whether the significant blow, if any, actually did occur at the time claimed. This last consideration can be disposed of first. It is more a matter of judicial than medical investigation and the doctor should ordinarily accept the patient's statement in this regard pending correction or verification by proper authority. He should avoid putting himself in the position of an insurance or similar investigator and leave that phase of the problem to those whose opportunities and training equip them to do it properly. Assessment of responsibility among repeated craniocerebral injuries will occasionally be necessary of course, but no general rule can be laid down for these occasions. Each is individual and will necessitate making available to the physician all the material that is germane to the problem before he can even approximate a decision. The verification of the date of the accident did not arise in this series of 50 patients. Judicial action by the Industrial Accident Board had identified the time and place of accident in every instance. There was a history of multiple craniocerebral injuries in only one case. No difficulty was met with in establishing the sig-

nificant accident—which proved to be the second—because the patient volunteered the information that he had been completely well and doing full-time work in the interval between the two. He was classed in the posttraumatic-state group because his symptoms were believed to be nonorganic in origin.

LOCAL OBJECTIVE EVIDENCE OF THE INJURY

To determine whether or not the patient has actually struck or been struck on his head may at times be very difficult. This will be especially true in the absence of visible or palpable signs and may involve check interviews with witnesses that one would not ordinarily see. Scars, and the like, on the scalp will be indicative, but not necessarily conclusive, evidence of this fact, inasmuch as the age of a completely organized scar cannot be accurately estimated and certain patients may use the scar from a previous accident to bolster their claims for damages on account of a later injury. Positive and negative roentgenograms of the skull must also be accepted with caution as final evidence for or against injury sustained at a given time. In the first place, my experience leads me to believe that in a disputed case certain differentiation of a fracture line from a blood vessel marking or suture line cannot be made without stereoscopic lateral roentgenograms, at the very least. Furthermore, to demonstrate such a differentiation, the films must be viewed in a stereoscope and not one-by-one in their flat state. Further confusion is caused by the fact that the rate and amount of bony union of linear fractures of the skull are completely unpredictable. It is true that, in general, such fractures that occur in children and young adults tend to heal quickly—in a matter of weeks—whereas similar fractures in the skulls of the elderly tend never to heal by bony union. Thus, in the first instance a roentgenogram that is positive at the time of injury may be negative when repeated at the time the patient is to appear in court. Presentation in evidence of only the latter film, with the suggestion that because it was negative the former was misread, would not, necessarily, be in accord with the truth, and might work a grave injustice on the complainant. On the other hand, it is possible to do the respondent an injustice also if the suggestion, that because a linear fracture remains visible roentgenologically after months or years, and hence is evidence in itself of a continuing cause of symptoms, is not branded as false and without basis in fact. In this group of 50 patients 25 showed positive evidence of head injury at the time claimed, in the form of the scar of a scalp wound or the demonstration of a fracture of the skull roentgenologically. Of these 25, ten were in patients whose symptoms were believed to be on an organic basis, and traceable to the injury, nine were in those with symptoms on a posttraumatic-state or nonorganic basis, two occurred in patients with a double diagnosis, two were noted in patients in whom no disease could be demonstrated, and in one the symptoms found at the time of the examination were believed to have been caused by an

CRANIOCEREBRAL INJURIES

intercurrent disease. In contradistinction to this, five of the organic, nine of the posttraumatic-state, two with a double diagnosis, four with no disease, and five with an intercurrent disease showed no evidence of either a scalp wound or fracture, and any conclusions as to the actuality of the blow in these patients had to be drawn from other evidence. Insofar as these figures go, and this is borne out by my experience in other cases, one may conclude that a scalp wound or properly identified fracture of the skull is good, but neither essential nor conclusive, evidence in support of a claim that present symptoms have a background of a preexisting blow on the head. In the absence of such a demonstration, recourse must be had to the history and to other objective physical findings of trouble with the central nervous system. In this connection, it seems probable that if the patient's symptoms, as complained of at the time of the examination, are traceable either to an intercurrent disease or an organic as opposed to a psychogenic cause, there will be found at examination to be positive objective physical signs of such disease or injury.

THE INTRACRANIAL EFFECT OF THE INJURY

The next decision that has to be reached, once the examiner is convinced that the claimant actually did strike his head, is whether or not the blow was sufficiently severe to produce intracranial pathology. Intracranial rather than cranial pathology is specified because any damage to the skull that does not simultaneously, or later, affect the skull contents—with the exception of the rare unrecognized compound fracture that becomes septic—will not produce late symptoms that have any direct cause and effect relationship to the alleged injury. Evidence that justifies the opinion that there has been such significant cerebral damage inflicted at the time of the injury, and that, therefore, the present symptoms can be correlated in a cause and effect relation to that damage is, for all practical purposes, concerned with the demonstration of loss of consciousness as the direct result of, and at the time of, the receipt of the alleged blow. It is true, as Denny-Brown and Russell⁸ have shown experimentally, that loss of consciousness is traceable to acceleration and/or deceleration of the head, and that, therefore, it is possible to visualize a situation in which lethal brain damage might be caused without such loss. In support of this view, Denny-Brown⁹ has instanced slow crushing of the head and penetrating wounds of the skull and brain by small missiles, usually multiple, and with very little inherent energy, either of which type of injury can and has caused sufficient brain damage to serve as the origin of late symptoms. I, too, have observed such a sequence of events following both a crush and stab wounds of the skull. When these latter accidents occur, however, there is no doubt in anybody's mind relative to the actuality of such an alleged fact, and confirmation of the significance of the intracranial damage is not necessary by other means. Penetrating wounds made by small low-energy fragments, such as follow bomb or similar explosions, are not ordinarily seen in the absence of a war, and

are easily recognized from the history as a possible cause for the complainant's symptoms. The only other source of error arises from the presence of a solid subdural hematoma resulting from the rupture of a bridging vein. The injury causing this may be so slight as not to be accompanied by unconsciousness. The clot in these patients will produce symptoms which vary from a mild but persistent headache to those usually associated with large brain tumors. A differential diagnosis between such a clot and a brain tumor is impossible without operative visualization. Patients with these symptoms and signs will usually prove to be such baffling problems that hospitalization, with a diagnostic study by all the means at hand, including pneumo-encephalogram, will prove necessary before the physician is justified in expressing an opinion relative to the cause-and-effect relationship between the accident and alleged resultant symptoms. Fortunately, these clots are rare—indeed the rarest of all subdural hematomata—and, therefore, one of the rarest of the intracranial complications of head injury. I¹⁰ have shown that chronic solid subdural hematomata occurred only 45 times in a series of 310 verified cases of all types of such clots. Furthermore, in only three of these 45 clots could a diagnosis of "brain injury" be made or a fracture of the skull demonstrated. Since the estimated occurrence of all subdural hematomata varies from one per cent (Browder, *et al.*¹¹), to my¹⁰ estimate of ten per cent, and since the occurrence of this particular solid type of clot is only 14 per cent of that, it is evident that the mathematical chance of finding one of these lesions as the cause of the claimant's symptoms is very small indeed.

LOSS OF CONSCIOUSNESS AND AMNESIA

Consciousness and, hence, unconsciousness are difficult to define satisfactorily. Seven types have recently been described by Miller,¹² who also gives 16 definitions of the word. I prefer Cobb's¹³ definition, in which consciousness is described as awareness of, and intellectual contact with, the individual's surroundings. This is highly variable from person-to-person and from time-to-time in any one person, and it is probable that, in the last analysis, no person is ever wholly conscious. Loss of consciousness, moreover, is not a definite entity as to time or amount. It merely implies a decreased awareness of his surroundings by the individual suffering from this phenomenon. This may be described in such terms as "dazed," "fainted," "groggy," "woozy," or "dizzy," to indicate the short periods, and as all the varieties of coma to indicate the longer ones. The demonstration of such a decrease in the patient's awareness of his surroundings may be extremely difficult and tax the ingenuity of the examiner to the utmost. One of the more reliable methods of verifying the presence of such a phenomenon is to investigate the patient's loss of memory in its relationship to the period before, during and after the accident. Retrograde amnesia—that is, a loss of memory for events that preceded the accident—especially if it is associated with accidental and anterograde amnesia is, in my experience, pathognomonic

of a loss of consciousness which is attributable to the accident. It cannot be confused with a similar condition caused by syncope, and offers opportunities for factual verification that will expose the malingerer. Amnesia that includes the time during which the accident was taking place and a period of time following it, but not necessarily including the actual start of the fall or receipt of the blow, is presumptive evidence of loss of consciousness. Postaccidental amnesia alone is, of itself, no evidence for or against loss of consciousness when it is not associated with either retrograde or accidental amnesia. Its significance depends upon its relationship to other factors in the case. The examiner should not be confused or jump to wrong conclusions because there may be a period immediately following the accident during which the patient talks and acts normally or because the patient has "islands of consciousness" in the sea of unconsciousness. Neither of these phenomena alter the diagnostic or prognostic significance of the unconscious period. I have seen an airplane pilot who crashed with a "dead stick" from 5000 feet. When rescued he was stepping out of the plane. He was taken by automobile five miles to a hospital, and during this trip told in detail how he had landed his ship without killing himself. On arrival at the hospital he became comatose, and for four days responded only to painful stimuli. At the end of that time he was again mentally normal, conscious, and in full contact with his environment. He was then asked to redescribe the landing of his plane but was unable to do so, and had no memory of anything from the time his engine failed at 5000 feet to the time he regained touch with his environment four days later. He was shown to have suffered a fractured skull, lacerated and contused wounds of the scalp, a contused brain, and other less serious injuries. Squadron Leader H. L. Burton,¹⁴ of the Royal Air Force, has also described this sequence of events as of sufficient importance to justify the medical personnel of the Royal Air Force, when investigating injuries sustained by pilots in "crashes" or by the riders of motorcycles in collisions, in obtaining the story of the loss of consciousness not only at once after the accident but some hours later as well. In this group of 50 patients (Table I) 33 had a history of loss of

TABLE I
UNCONSCIOUSNESS AND AMNESIA

		Organic	Post-traumatic- State	Inter-current Disease	No Disease	Double Diagnosis	?	Totals
Unconsciousness	{ Yes.....	12	11	0	5	4	1	33
	{ No.....	0	5	6	1	0	0	12
	{ ?.....	3	2	0	0	0	0	5
Amnesia	{ None.....	0	6	6	3	0	0	15
	{ Retrograde.....	0	5	0	0	0	1	6
	{ Postaccidental	12	11	0	3	4	1	31
		3	1	0	0	0	0	4

consciousness, 12 had no loss of consciousness, and in five there was doubt as to this fact. Among those shown to have been unconscious, 12 had symptoms that were classed as organic, those of 11 were considered to be non-

organic, those of four were traceable to the combination of two conditions, and in five it was felt that no disease was present when they were seen later. Five of the posttraumatic-state group, six with intercurrent, and one with no disease, were considered not to have been unconscious. In regard to the incidence of the various kinds of amnesia there were 12 patients with postaccidental, three who might or might not have had any kind of amnesia, and none who did not have some loss of memory among the "organic" group. Language difficulties accounted for the three undetermined cases. Among those whose symptoms were classed as posttraumatic-state or on a nonorganic basis, five had retrograde, 11 had postaccidental, one could not be determined, and six had no amnesia. Four patients who had a combination of organic symptoms and intercurrent disease as a basis for their symptoms had postaccidental amnesia, six who were suffering from an intercurrent disease alone had no amnesia, six that had no disease were equally divided between postaccidental and no amnesia, and one patient, that could not be classified, had a combination of retrograde and postaccidental loss of memory, as did five of the posttraumatic-state group already listed. There was no evidence of any original intracranial injury in any of the patients in the intercurrent disease group. It seems reasonable to conclude that unconsciousness at the time of the injury predicates intracranial pathology sufficient to serve as an adequate cause for the production of late symptoms. On the other hand lack of unconsciousness at the time of the original injury can be taken to indicate that any late symptoms are almost certainly either traceable to a functional nonorganic upset or are caused by an intercurrent disease. All patients who were certainly known to have been rendered unconscious originally, gave a history later on of some type of amnesia, which was usually postaccidental.

CLASSIFICATION OF THE SIGNS AND SYMPTOMS OF LATE DISABILITY

Having verified, or failed to verify, the claimant's allegation that he was struck on the head at the time of the alleged accident sufficiently hard to cause intracranial damage, one must now make some attempt to tabulate and classify the myriad symptomatology that the patient is only too willing to describe. Care should be taken never to ask direct questions or to otherwise suggest by naming it any particular symptom. All these patients are highly suggestible and ready to adopt as their own almost any symptom that is brought to their attention. I have never believed that there is any special diagnostic value to be found in the characteristics of purely subjective symptoms. Objective signs however, even if described as symptoms, are different. Some demonstrable pathology can be found behind such symptoms in practically every instance if the examination be sufficiently detailed and searching. This is not to be taken to mean that subjective symptoms are without significance. It is merely that that significance must be interpreted in the light of other and objective data, whereas objective signs have their interpretation inherent in them. In addition to the abnormalities found in physical and neurologic examination, the 50 patients in this group com-

CRANIOCEREBRAL INJURIES

plained voluntarily of 17 symptoms. Because the number of other such possibilities is practically legion only these 17 will be considered here. They are fairly representative of the larger group, and I believe that conclusions reached from their analysis will hold true for the rest.

OBJECTIVE SYMPTOMATOLOGY

If the abnormalities found in physical and neurologic examinations are excluded, four such symptoms fall in the objective group (Table II). These are convulsions; loss of memory or change in personality; paralysis of one or more extremities; and loss of weight. In addition, physical abnormalities demonstrated at general physical and neurologic examinations, and excluding scars of scalp wounds or fractures of the skull, were present in 13 of 15 in the organic, both patients who were classed as belonging in the double diagnosis group (a combination of organic and intercurrent disease), and in all five of the patients with intercurrent disease. Two organic cases,

TABLE II
OBJECTIVE SIGNS AND SYMPTOMS

	Organic	Post-traumatic-State	Inter-current Disease	No Disease	Double Diagnosis	?	Totals
Scalp wound or fracture { Yes..... No.....	10 5	9 1	1 5	2 4	2 2	1 0	25 25
Other physical signs { Yes..... No.....	13 3	9 17	1 5	2 0	2 2	1 1	22 28
No physical signs at all.....	0	9	0	0	0	0	11
Convulsions.....	4	1	2	1	1	1	10
Loss of memory or personality change...	4	0	0	0	0	0	2
Paralysis of extremity.....	0	3	1	0	0	0	4
Loss of weight.....	0	1	0	0	0	0	1

who had no abnormal physical signs, had convulsive seizures that developed as the direct result of the earlier injury. The two patients with no disease, and nine out of 18 patients in the posttraumatic-state group had no abnormal physical signs. Convulsions were present nine times—four among the organic, two in the intercurrent disease group, and one each in the post-traumatic, double diagnosis and unclassified groups. Loss of memory or change in personality occurred 10 times—four each in the organic and post-traumatic-state, once in the double diagnosis, and once in the unclassified groups. Three patients who were reexamined were found to have a change in personality at the second but not at the first examination. Two of these were in the organic, and one in the intercurrent disease group. While it is unfortunately true that although the disability claimed by a patient as the late result of an antecedent accident need not result from an objective physical defect, the very fact that such a defect is present puts the burden of proof on the examiner to show that it is not the causative factor. No greater significance than that can be attached to the demonstration of abnormal physical signs and what may be spoken of as objective symptomatology in a consideration of the relationship between an antecedent craniocerebral injury and later disability.

SUBJECTIVE SYMPTOMATOLOGY

Subjective symptomatology that is allegedly the cause of late disability in craniocerebral injuries is the most difficult part of this whole problem to evaluate. The possible causes of headache, insomnia, dizziness when stooping, general pains, and the like, are legion. There is no present evidence to show what the statistical chance of their occurrence is, in either normal persons or in those afflicted with the various cerebral changes that follow craniocerebral injuries. A patient with a known psychopathic personality, and an imaginary craniocerebral injury, will, and often does, complain of the same symptoms and the same disability that another with a fluid subdural hematoma following a severe injury, or still another with generalized cerebral atrophy that has followed a mild injury in an arteriosclerotic does. To separate each from the others will require a knowledge of the pretraumatic personality of the patient, a detailed study of his personality and state of physical health at the time of the complaint, an objectively accurate diagnosis of the pathology present at the time of the injury, and in the case of the atrophy a pneumo-encephalogram, and in that of the subdural fluid hematoma an exploratory operation before the differential diagnosis can be made, and the cause-and-effect relationship between the accident and the disability unravelled. Even this may not give the full explanation because, for example, in the hematoma case an associated neurosis may still persist after the correction of the physical abnormality. When such symptoms remain a demand will be made on the doctor to divide the responsibility for this continued disability between a possible instability of the patient's pretraumatic personality, the changes induced by an unfavorable environment before or after the injury and the still persisting effects of an intracranial abnormality that may have been present for some weeks or months.¹⁵ Other even more complicated relationships can be easily visualized, and the hopelessness of reaching a just conclusion relative to the importance of such subjective symptomatology as a cause of late disability after previous craniocerebral injuries can be realized. Much psychometric, social service, psychiatric, psychologic, neurologic, pathologic and surgical data relative to the acute as well as the more prolonged effects of all varieties of craniocerebral injuries must be collected before the significance of this class of late symptoms can be evaluated or even recognized as existing. Headache, dizziness on stooping, and general weakness were the commonest of this class of symptoms in this group of 50 patients (Table III). Forty-four of the 50 had headaches, 28 dizziness, and 16 general weakness. Of the six patients who had no headaches, one each out of 15, and 18, respectively, were in the organic and posttraumatic-state, and two each out of six in both the intercurrent and no disease groups. Thirteen of the 15 organic, eight of the 18 posttraumatic-state, one-half of the intercurrent disease and double diagnosis, and one-third of the no disease groups complained of dizziness on stooping. Seven of the organic, five of the posttraumatic, two of the intercurrent disease,

and one each of the no disease and double diagnosis groups, complained of generalized weakness. Nervousness (13 times), and insomnia (12 times), were the next most common. They were as common in the organic as they were in the posttraumatic-state group. The frequency and classification of the rest is noted in Table III. The English school^{2, 3, 4, 5, 6, 8, 9} has shown that before conclusions could be drawn relative to the relationship between such symptoms and their antecedent accidents, as occurred among casualties in the Royal Air Force, information relative to the patient's personality, home life, relation to environment, work record, intellectual level, and the like, had all to be collected for both the time preceding and that succeeding the accident. This was possible without undue expenditure of time, money and personnel in this British group. It would not be possible in the ordinary industrial or automobile accident case in this country. However, that does not imply that such investigation should be altogether neglected. As much of this information as is possible should be acquired in every patient. A

TABLE III
SUBJECTIVE SYMPTOMS

	Organic	Post-traumatic-State	Inter-current Disease	No Disease	Double Diagnosis	?	Totals
Headache { Yes.....	14	17	4	4	4	1	44
{ No.....	1	1	2	2	0	0	6
Dizziness on stooping.....	13	8	3	2	2		28
Weakness.....	7	5	2	1	1	0	16
Nervousness.....	6	4	1	1	0	1	13
Insomnia.....	5	4	1	2	0	0	12
Pressure in the head.....	5	2	1	1	1	0	10
Inability to concentrate.....	5	2	1	1	0	0	9
Noise in the ears.....	6	2	1	0	0	0	9
Difficulty with sight.....	3	4	0	0	0	0	7
Photophobia.....	2	1	0	0	0	0	3
Increase of symptoms in wet weather...	1	1	1	0	0	0	3
Intolerance of noise.....	2	1	0	0	0	0	3
Confusion in crowds.....	1	1	0	0	0	0	2

family history of insanity, epilepsy, sick headaches or conditions similar to the one from which the patient suffers, evidences of marital incompatibility, addiction to alcohol or drugs either in the family or on the part of the patient, will help clarify the patient's emotional background and permit an estimate of his pretraumatic personality to be made. His work record, including the frequency with which he changes jobs, the number of his promotions and the reasons or lack of reasons there-for, give further insight. A review of his educational background, a knowledge of the country from which he or his family originated, and observations on his emotional reactions while undergoing examination, are all additional helpful data that can be obtained with little or no extended investigation. Finally, such evidences of an over-sensitive sympathetic nervous system as cold and discolored extremities, excessive sweating, fainting, irregular pulse, dermatographia, "goose-flesh," and the like, may well provide the clue to otherwise unexplainable symptomatology and permit recognition of the fact that the disability claimed arises not from the antecedent accident but rather from emotional or psychic deficiencies in-

herent in the victim. All such data as can be obtained in the present state of our knowledge from a study of the above and other subjective symptoms, is to the effect that when any one of such symptoms acts, of itself, as the chief cause of late disability following an earlier craniocerebral injury it is of no value either for diagnostic purposes or for determining the cause-and-effect relationship between the accident and the later disability. The only positive virtue that its presence affords is in forcing the physician to use all possible methods of diagnostic investigation if he would really determine the reason for and the significance of it.

EFFECT OF EARLIER THERAPY

One other possible variant must be briefly mentioned: Its effect is impossible to estimate and yet is a real factor in the prolongation of disability and in its influence on the patient's morale and later subjective symptomatic reactions. It is the efficiency of the treatment rendered at the time of the accident. As was pointed out in the first section of this paper, this is intimately connected with the accuracy of the original diagnosis. A subdural hematoma that is promptly recognized and removed will cause less permanent cerebral changes and, hence, less later disability than one that is not recognized and removed for some months and until the late disability has already developed. A lacerated brain that is diagnosed and treated as a case of concussion falls into the same category. Moreover, a true case of concussion that is forced to undergo a prolonged convalescence because the doctor has mistakenly considered it a "serious brain injury" has the cards stacked against him, and will inevitably develop a neurosis and disabling symptoms sufficient in number to justify to himself, his friends and family the fact that, although acting and feeling well, he is nevertheless an invalid. In only one of the 50 cases reported herewith, was it possible to state that sufficient objective data had been collected at the time of the accident to justify making a diagnosis in terms of pathology. As an inevitable result the immediate therapy left much to be desired and was usually conspicuous by its absence. Even those patients who had no disease at the time of their examination were well in spite of, and not because of, the therapy they had received earlier. The length and psychologic handling of the convalescence may also prove to be important factors in influencing the occurrence of later symptoms. I¹ have dealt with this elsewhere, and will only repeat that: "The convalescent care of patients with craniocerebral injuries should not be of a hit-or-miss type but must be carefully planned to keep the inevitable associated destruction of initiative and self-confidence from developing into a permanent neurosis, and spoiling the end-result of what might, otherwise, have been a successful case." In two of the patients in this series of 50, the symptoms and disability arising therefrom were unquestionably traceable in one case to a convalescence that was too prolonged and inactive, and in the other to one that was too short and active. Eleven of the 15 organic, 12 of the 18 posttraumatic, five of the six intercurrent

disease, and two of the four double diagnosis cases, were doing, and had done, since their injury no work and taken no exercise. One organic and one posttraumatic case worked about the house, and another of the latter group took moderate exercise. All the patients with no disease, three of the organic, four of the posttraumatic, the other two of the double diagnosis group, and one unclassified case were at work when seen.

THE INFLUENCE OF PENDING LITIGATION

The influence of pending litigation on the persistence of symptoms in these patients is a real but rather overstressed factor. The causes are obvious, and their elimination equally so. Four of the patients in this group of 50 had a coincidental complete recovery from their disability and the ending of litigation by settlement of their claims. Attention should be called to the fact that although such a coincidence is presumably due to something analogous to malingering it is not necessarily so. A patient with neurosis based upon dread of appearing in court will react similarly to one who fears injustice because of his inability to demonstrate the truth of his claim in the same surroundings. In such circumstances, these patients, like the malingerer, will recover from their disabilities with the ending of their litigation.

CLASSIFICATION OF THE DISABILITY

Before settling the question of cause-and-effect relation between the accident and later disability the patient must be classified as to the type of his disability. I have found it convenient to do this under five headings. These have been referred to previously in the body of this paper and are as follows: *Organic; posttraumatic-state; intercurrent disease; no disease* and *double diagnosis*.

In the *organic group* are classed those patients who sustained a significant blow on the head and who can be shown to have organic objective abnormalities that are not traceable to intercurrent disease, and that may occur either with or without functional subjective symptoms. The demonstration of such objective abnormalities usually will require hospitalization, often pneumoencephalography, and frequently bilateral exploratory trephination. Unless the demonstration in an office is unquestionable, the physician should not commit himself relative to this possibility without either qualifying his statements or having the benefit of such hospitalization. In this group of 50 patients there were 15 who were classed as organic. All were seen first in the office, and an unqualified diagnosis and opinion refused in 12 pending hospitalization. In most instances, for various reasons varying from the unwillingness of the patient to cooperate, to the influence of friends and financial stringency, the recommendation for hospitalization was not acceded to, and the qualified findings were accepted. It is my considered opinion that this was a mistake and should not have been permitted. Of the three for whom hospitalization was not recommended, and an unqualified diagnosis

and opinion rendered, two had been previously hospitalized, even to the extent of transtemporal exploration and in one sufficient objective evidence was amassed at the office examination to obviate further hospital study.

The *posttraumatic-state* group includes those patients who sustained a significant blow on the head but who at the time of the later examination do not have any organic objective abnormalities but do have functional subjective symptoms. The demonstration of such a lack of objective abnormalities cannot be considered final unless, and until, hospitalization with pneumo-encephalogram, and other similar tests, have proved normal. In some cases, particularly those about whom one has any doubt because of the length, persistence or disabling quality of the symptoms, bilateral exploratory trephination will have to be resorted to as well, before the doctor can make an unqualified diagnosis. It is this group of cases that includes all the most difficult problems relative to cause-and-effect relationship between the accident and disability. Often it will be impossible to be sure of this relationship and any information bearing on pretraumatic personality, personal relationships, environment, habits, illnesses, work record, *etc.*, is sure to be helpful. The family and educational history must be investigated, and a search for hereditary or obscure diseases, must also be carried out. With this, and similar information at hand, it will be possible in many cases to decide whether the claimed disability has actually been caused by the preceding accident or by an hitherto unsuspected, and perhaps inactive, effect of an abnormal pretraumatic personality or other personal peculiarities. To avoid confusion in nomenclature I have preferred to use the term *posttraumatic-state* for this group of symptoms. It has many other names, some without meaning, as *postconcussional-state*, and others, as *posttraumatic neurosis*, that are more descriptive than *posttraumatic-state*. The latter diagnoses imply too much however, and may be as harmful as the meaningless ones. In the 50 cases reported herewith there were 18 on whom this diagnosis was made. Four were first seen in the hospital and 14 in the office. Qualified diagnoses were made on five pending hospitalization. Unqualified diagnoses were made on nine others, none of whom were recommended for hospitalization. Two of these had become free of complaints and disability just prior to examination and following settlement of litigation about their claims. Two had hyperactive sympathetic nervous systems, without other symptoms. One of these was also of very low intelligence and extremely emotional. In two the symptoms were located in the region of the supra-orbital nerve but since the patients had probably been knocked unconscious by the blows which caused the bruises about their eyes, they were considered to have probably had a mild craniocerebral injury. They were included in this group despite the highly localized character of their symptoms. One other patient was alcoholic and another had a very bad work history, and, in addition, sustained her injury by jumping out of a window in an attempt to escape a fire in the factory where she worked. These were considered adequate causes

CRANIOCEREBRAL INJURIES

for later symptomatology. Finally, the ninth patient had had two previous hospitalizations, including exploratory trephination—all of which were negative—before I examined him.

The importance of recognizing that more than one diseased condition may be present, and that the combination may thus enhance the symptoms and disability inherent in either one cannot be overestimated. Omitting the obvious and fairly constant organic and posttraumatic-state relationship, it is in this group that the fruits of failure on the part of the employer to require preemployment and periodic physical examinations are collected. A craniocerebral injury causes enough disability when it occurs alone in a healthy individual. When the effects of a preexisting disease are added, the resulting disability may increase out of all proportion. This is especially true when the circulation is involved. Not only is the local damage produced at the time of the injury greater but treatment is less effectual. Worst of all, postinjury disability is greater, and in a large group of such patients is progressive also. Such patients are grouped under the heading *double diagnosis* which is self-explanatory. There were four patients among the 50 on whom a double diagnosis was made. All had a combination of objective organic signs, part of which were traceable to the original craniocerebral injury, and part to an associated intercurrent disease. In every case this intercurrent disease was vascular—either arteriosclerosis with hypertension or hypertension alone. One was seen originally in the hospital and the other three in the office. Hospitalization was not considered necessary in these latter because two had already been hospitalized and adequately studied elsewhere, and there was sufficient data collected from the office examination of the other to make the diagnosis unquestionable.

Patients whose disability is thought to be caused by intercurrent disease or who, at examination, have no disability are classified under the headings *intercurrent disease* and *no disease*. The first of these conditions should never be overlooked in any patient even though he himself may believe the symptoms to have been entirely caused by the original craniocerebral injury. The problem in such cases is not to recognize the fact that an intercurrent disease is present—once one remembers that possibility—but rather to decide whether the individual patient belongs in this grouping rather than in the double diagnosis classification. In the former the disability will be independent of, and in no way influenced by, any preexisting craniocerebral injury. In the latter, as pointed out above, the two are interdependent. Each such problem is an individual one and subject to no general rules for its solution. There were six such patients in this group. One was first seen in the hospital, two were advised to enter the hospital for confirmation of their diagnoses, and three presented such typical findings in the office that hospital examination was not considered necessary.

Patients classed as having *no disease* are usually those who want permission to return to work, or whose counsel want their client's medical con-

dition verified before reaching a final settlement of the litigation. The reasons for the classification are self-explanatory.

CRITERIA NECESSARY TO LINK ANTECEDENT CRANIOCEREBRAL INJURY AND LATER DISABILITY

It must now be apparent that certain criteria have to be met before the doctor is justified in giving, or the lawyer in accepting, an opinion relative to the relationship between a craniocerebral injury and later an allegedly consequential disability. Such an opinion can be unqualified only after the patient has submitted himself to an investigation that will demonstrate the significance of all objective findings and will give proper consideration to all the inherited, personal, social, educational and occupational influences that have been brought to bear upon his personality both before and after the alleged injury. If these requirements cannot be, or are not, satisfied then the opinion referred to above must be qualified appropriately.

If the opinion is to be sustained that a direct cause-and-effect relationship exists between the injury and the later disability, the following criteria must be met: 1. That a patient actually did sustain a blow on the head at the time and place claimed. 2. That that blow was sufficiently significant to produce intracranial pathology at the time of its infliction. 3. That the disability be manifested by organic signs and symptoms that could only arise from earlier and continuing intracranial pathology. 4. That the disability be manifested by a combination of organic signs and symptoms that could only arise from intracranial pathology, and the signs and symptoms of intercurrent disease or the subjective symptoms seen in the so-called post-traumatic-state. 5. That in the absence of objective signs any subjective symptoms complained of be shown after adequate investigation not to be, or have been, caused by any characteristics found in the patient's pretraumatic personality, and its changes, or in his inheritance or his social, family, intellectual, emotional, or work history.

If the opinion is to be sustained that there is no direct or indirect cause and effect relationship between the claimed injury and the later disability the following criteria must be met: 1. That the patient may or may not have sustained a blow on the head at the time and place claimed. 2. That if such a blow was sustained it was not sufficiently significant to produce any intracranial pathology at the time of its infliction. 3. That there be no organic signs or symptoms found after a sufficient search which could reasonably be supposed to arise from an earlier and continuing intracranial pathology. 4. That any organic signs or symptoms that are present be most reasonably explained on the basis of an intercurrent disease. 5. That any subjective symptoms present be most reasonably explained on the basis of characteristics found in the patient's pretraumatic personality, and its changes, or in his inheritance or his social, family, intellectual, emotional, or work history.

It is the function of the court, or of an insurance or similar investigator, to verify the time and place of the alleged injury. Scars of scalp wounds,

CRANIOCEREBRAL INJURIES

bruises and properly checked skull fractures can verify its actuality. The demonstration of a period of unconsciousness verified by amnesia before, during or after the injury, or the presence of a solid cerebral subdural hematoma, perforating wound or wounds of the skull and brain, or a crushed skull, will verify the significance of this injury. The classification of the signs and symptoms into those caused by organic changes that have originated in either the injury or an intercurrent disease, or both, and those that are purely subjective and are either traceable to the functional as opposed to the organic effects of the injury or to characteristics found in the patient's pretraumatic personality and its changes, or in his inheritance or his social, family, intellectual, emotional, or work history, will permit a reasonably accurate estimate of the cause-and-effect relationship between the alleged cranio-cerebral injury and any succeeding disability.

REFERENCES

- ¹ Munro, D.: Convalescent Care of Patients with Craniocerebral Injuries. *N. E. Jour. of Med.*, 220, 1023-1026, 1939.
- ² Denny-Brown, D.: The Sequelae of War Head Injuries. *N. E. Jour. of Med.*, 227, 771-780 and 813-821, 1942.
- ³ Symonds, C. P.: *Proc. Roy. Soc. Med.*, July, 1942.
- ⁴ Jefferson, G., Cairns, H., and Brain, W. R.: Discussion on Rehabilitation after Injuries to the Central Nervous System. *Proc. Roy. Soc. Med.*, 35, 295-308, 1942.
- ⁵ Cairns, H.: Treatment of Head Injuries in War. *Brit. M. J.*, 1, 1029, 1940; *idem*: Gunshot Wounds of the Head in 1940. *J. Roy. Army M. Corps*, 76, 12-22, 1941.
- ⁶ Symonds, C. P.: Observation on the Differential Diagnosis and Treatment of Cerebral States Consequent upon Head Injuries. *Brit. M. J.*, 2, 829-832, 1928.
- ⁷ Munro, D.: Craniocerebral Injuries. Oxford Univ. Press, N. Y., pp. 412, 1938.
- ⁸ Denny-Brown, D., and Russell, W. R.: Experimental Cerebral Concussion. *Brain*, 64, 93-164, 1941.
- ⁹ Denny-Brown, D.: Delayed Collapse after Head Injury. *Lancet*, 1, 371-375, 1941.
- ¹⁰ Munro, D.: Cerebral Subdural Hematomas: A Study of 310 Verified Cases. *N. E. Jour. Med.*, 227, 87-95, 1942.
- ¹¹ Landig, G. H., Browder, E. J., and Watson, R. A.: Subdural Hematoma: A Study of 143 Cases Encountered during a Five-year Period. *ANNALS OF SURGERY*, 113, 170-191, 1941.
- ¹² Miller, James G.: Unconsciousness. John Wiley and Sons, New York, pp. 329, 1942.
- ¹³ Cobb, Stanley: Foundations of Neuropsychiatry. Williams and Wilkins, Baltimore, pp. 231, 1941.
- ¹⁴ Burton, H. L.: Discussion on Minor Head Injuries. *Proc. Roy. Soc. Med.*, 24, 1405-1410, 1931.
- ¹⁵ Munro, D.: The Diagnosis and Therapy of So-called Posttraumatic Neurosis following Craniocerebral Injuries. *Surg., Gynec., and Obst.*, 68, 587-592, 1939.

MECHANISMS OF HEAD INJURY

ALAN R. MORITZ, M.D.

BOSTON, MASS.

FROM THE DEPARTMENT OF LEGAL MEDICINE, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

INJURIES OF THE HEAD probably account for more deaths leading to litigation of one kind or another than does any other one category of mechanical trauma. Not only are such injuries responsible for a large proportion of all deaths by violence but they are also a common cause of non-fatal disability. When indemnification is claimed or assault is charged on a basis of such an injury, it is obviously desirable that the medical witness understands the various mechanisms by which physical forces may result in damage to the head and its contents.

Although mechanical injuries of the head may be produced in many different ways they are due, in the last analysis, to the application of force in such a manner that it changes or tends to change the state of rest or uniform motion of the structures affected. Thus, the impact responsible for injury may result from a collision between a stationary head and a moving object, a stationary object and a moving head, or a moving head and a moving object when either the direction or the rate of motion of the two is different. The site of the collision may be on the external surface of the head itself or the force of a collision occurring elsewhere on the surface of the body may be transmitted to the head by way of the spine.

Although the precise manner in which some of the mechanical disturbances of the brain are brought about is obscure, it has long been recognized that certain types of external force tend to cause more or less characteristic injuries. Thus, if the nature of the alleged accident or assault is known, it may be possible to predict the particular kind of structural or functional disturbance that is likely to have been sustained. Conversely, if the nature of the disturbance is known it may be possible to reconstruct the probable manner in which it was produced.

An injury of the head may involve the scalp, the skull, the meninges, or the brain itself. These structures may be involved singly or in any combination. Obviously, the principal significance of a head injury lies in the extent to which the brain is or will subsequently be affected. It may be damaged immediately by the disruptive mechanical force of the impact or it may be affected some time later because of damage done to the skull or to the meninges. It is important to bear in mind that severe and even fatal damage to the brain may be sustained without significant injury to the scalp or skull. Conversely, extensive damage to the scalp or skull may be sustained without concomitant injury to the brain. The inac-

MECHANISMS OF HEAD INJURY

curate characterization of an injury in which the brain has been damaged simply as a skull fracture is as regrettable as it is common.

INJURIES OF THE SCALP

The principal significance of a wound of the scalp in relation to the general problem of head injury lies in the fact that it provides objective evidence that force has been applied to the head. To the experienced observer it may indicate not only the direction in which the force was traveling but it may also disclose the character of the instrument or object that produced it.

Undoubtedly, the most susceptible large skin area of the body to disruption by blunt impact is the scalp. This is due to the fact that nowhere else in the body is such a broad expanse of skin separated from the underlying bone by so thin a cushion of soft tissue. In most situations the skin

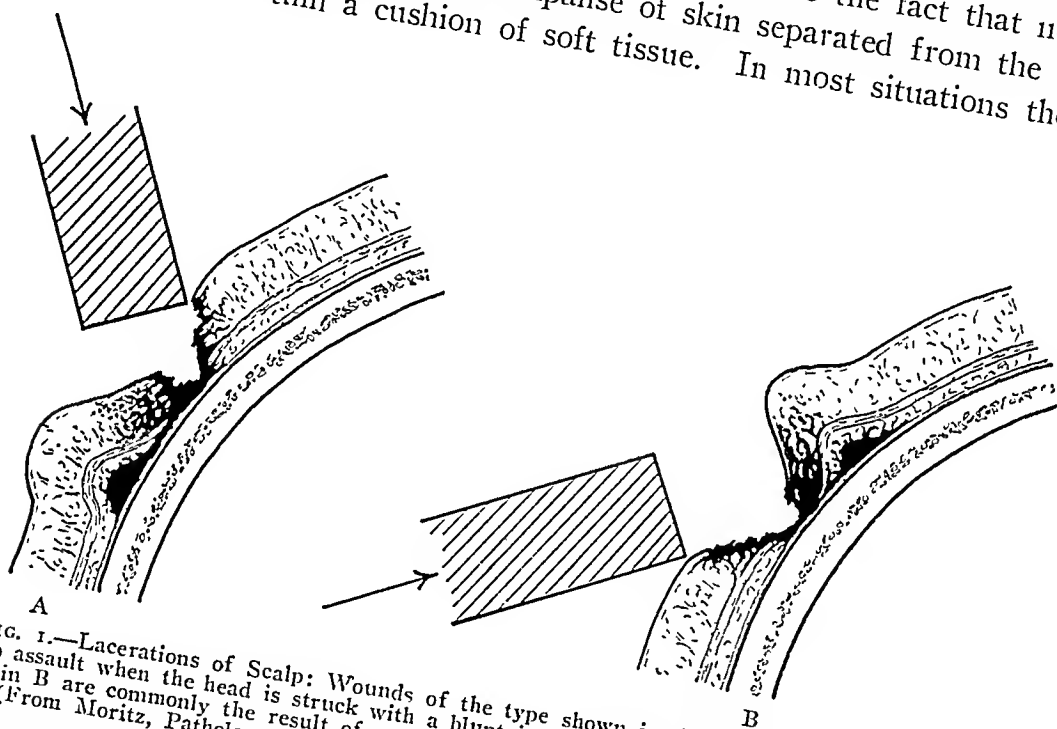


FIG. 1.—Lacerations of Scalp: Wounds of the type shown in A are commonly produced incident to assault when the head is struck with a blunt instrument from above. Wounds of the type shown in B are commonly the result of a fall in which the downward moving head meets resistance. (From Moritz, Pathology of Trauma, Courtesy of Lea & Febiger)

is well cushioned by fat or muscle so that an impact is likely to be decelerated slowly but this is true only to a very limited extent in the case of the scalp. Because the skull is curved, the force of an impact is frequently deflected and the scalp is accordingly stretched and torn. Characteristically such lacerations tend to occur at right angles to the direction of the impact. Careful examination will usually disclose the direction of the impact by the manner in which the scalp has been torn from the skull. Thus in the case of a glancing blow from above the lower margin of the laceration is likely to be undermined and separated from the bone. In the case of an impact from below such as occurs when a person slips and falls to the ground, the upper margin of the laceration is likely to be undermined (Fig. 1). If the head is struck at an angle by a small object, a narrow tongue or three cornered flap of the scalp is likely to be torn loose. The

apex of the flap will mark the site of the initial impact. If the area of a glancing impact is large as much as half of the scalp may be torn from the skull.

Case 1.—The wife of a disoriented and agitated inmate of a mental hospital complained that her husband had been brutally assaulted by an attendant. A nurse had found her husband on the floor of his room in an unconscious state and bleeding from a deep wound of the scalp. The accused attendant stated that the patient was all right about two hours prior to the time that his injury was discovered, at which time he had brought the patient a bedpan. The wife stated that her husband had frequently complained that this attendant had threatened him with a club and that she had personally observed that the attendant was impatient and rough with his charges. She felt sure that the attendant had struck her husband on the head on the morning in question.

An examination of the scalp wound revealed that the force responsible for it had been traveling upward. An inspection of the premises disclosed that the injury had undoubtedly been sustained as a result of a fall in which the patient had struck the back of his head against the edge of a chair. This impression was strengthened by the fact that the injured man was known to be the subject of frequent fainting spells. Although the evidence upon which the wife based her charges was at no time strong, it was gratifying that the medical findings were sufficiently definitive to dispose of the case to the satisfaction of both the wife and the hospital authorities.

The nature of the object responsible for an injury of the scalp can frequently be recognized by the shape of the wound. Thus, the imprint left by a tire tread, by the grill of a radiator, by the head of a hammer, or by any one of a number of other objects may be clearly delineated by the pattern of the wound.

Case 2.—A maid left in charge of a town house was found dead on the floor by her employers when they returned from a week-end at the shore. She had been the victim of rape and had died as a result of head injury. Examination of the scalp and skull disclosed the fact that she had been struck repeatedly with an instrument having a triangular striking surface, the sides of which measured about one and one-quarter inches in length. The police investigation was directed to the finding of an instrument answering to this description. A blood-stained mason's hammer, the head of which corresponded to the size and shape of the wounds, was eventually found beneath the back porch of a gardener's cottage on the grounds. The similarity between the peculiar head of the hammer and the contour of the wounds was an important evidential factor in the subsequent conviction of the gardener.

The finding of a recent bruise or laceration of the scalp of a person unconscious from unknown cause does not justify the assumption that unconsciousness was caused by mechanical injury. People who collapse so unexpectedly that they fall to the ground frequently sustain secondary head injury. More times than not, the injury received in such circumstances is inconsequential, although it may appear otherwise at first. It is by no means uncommon in the case of a person found unconscious with a bruise or laceration of the scalp to find that the true cause of the collapse was heart disease or spontaneous intracranial hemorrhage.

Case 3.—A man arrested at midnight for drunkenness and disorderly conduct was found dead on the floor of his cell on the following morning, with evidence of

MECHANISMS OF HEAD INJURY

recent bleeding from the nose and mouth and with a large bruise of the forehead. He had shown no external evidence of injury at the time of his arrest. Relatives charged that the deceased had been assaulted by the police and their allegation apparently was corroborated by the preliminary findings of the coroner who reported that in his opinion death had resulted from a traumatic subarachnoid hemorrhage.

Subsequent investigation of the brain by a qualified pathologist disclosed that the fatal hemorrhage had originated from a miliary aneurysm of the circle of Willis, that the bleeding from this aneurysm had been in progress for several days prior to death,

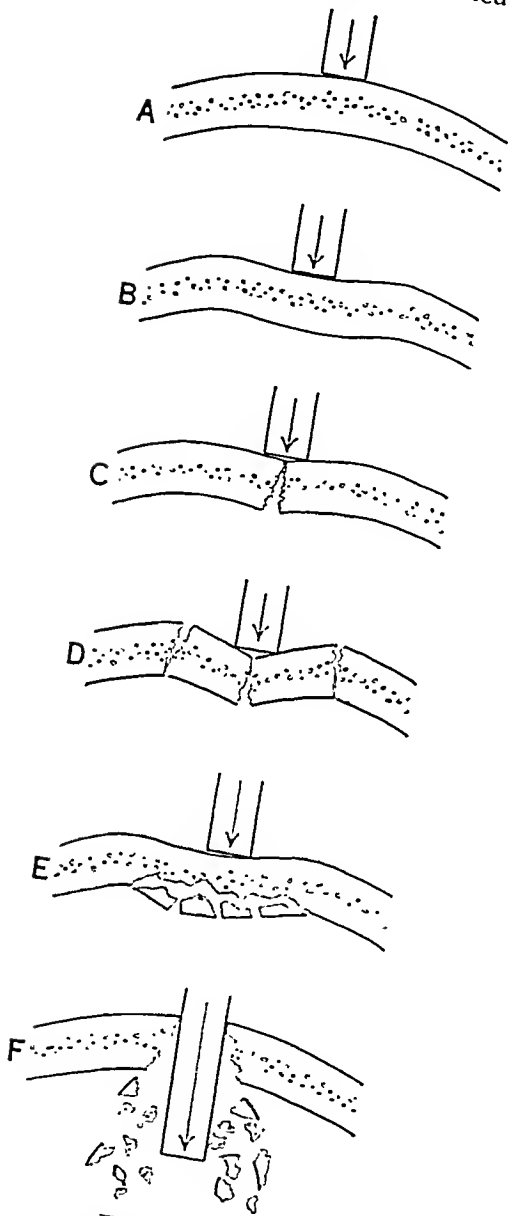


FIG. 2.

FIG. 2.—The Effects of Impact on the Skull: A. Before impact. B. Indentation or flattening, without fracture. C. Simple linear fracture. D. Comminuted fracture. E. Flaking of internal table (most commonly caused by glancing impact of bullet). F. Inverted crater (characteristic of penetrating bullet wound).

FIG. 3.—Schematic representation of characteristic sites of basilar fracture caused, respectively, by frontal, lateral, and occipital impacts.

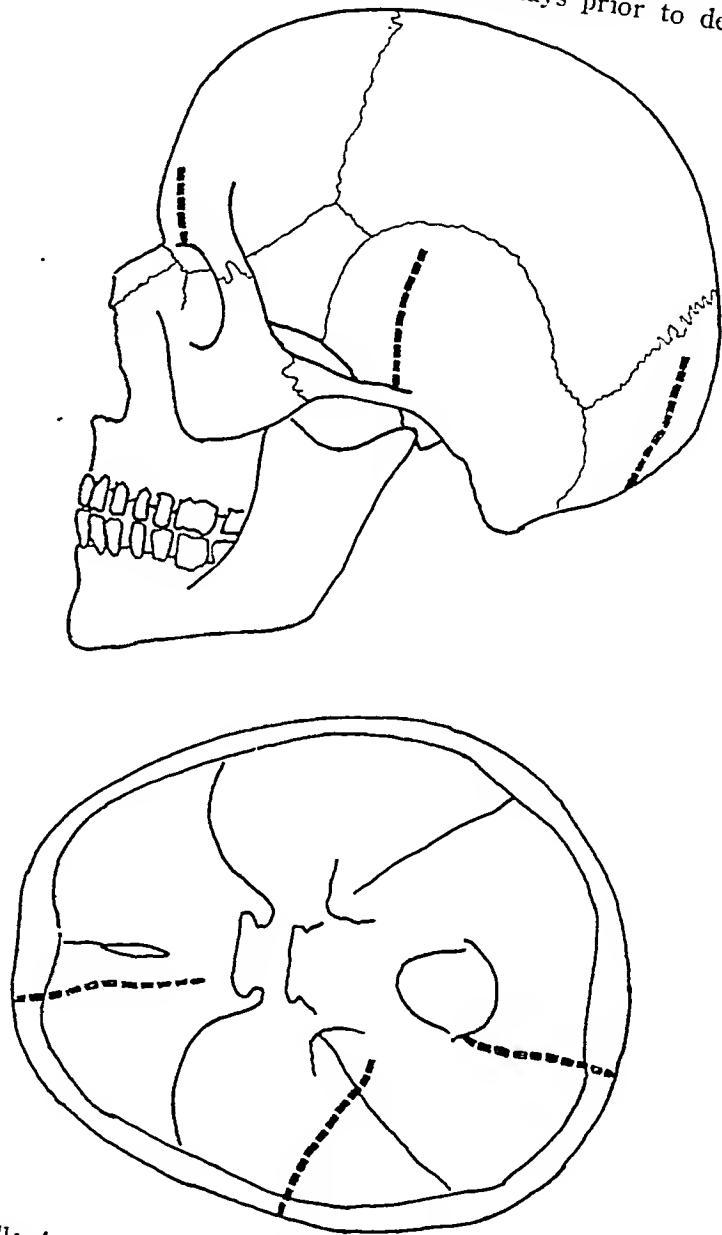


FIG. 3.

and that mechanical injury had no causal relation to its occurrence. It was concluded, therefore, that the decedent had probably been disturbed during the night by headache caused by the accumulation of blood within the subarachnoid space, had arisen from his cot, fainted, and collapsed face down on the stone floor of his cell with resulting bruising of nose, lips, and forehead. The charges against the police

were withdrawn. The seriousness of the injustice that might have resulted if the true significance of the medical evidence had not been recognized is apparent.

INJURIES OF THE SKULL

Whether the bone breaks at the site of, or remote from, the external impact depends largely on the velocity at which the collision occurs and on the local resistance of the skull. Often the only objective evidence bearing on the manner in which a fatal head injury has been sustained is disclosed by the location and character of the lines of fracture. This fact is of particular importance to the coroner or medical examiner who finds in about 20 per cent of all cases of fatal head injury investigated by him that the postmortem findings are the sole source of objective evidence relating to the manner in which the injury was incurred. In such instances the only reliable evidence bearing on such important medicolegal questions as the number of times the head was struck, the site at which and the violence with which the force was applied, and the size and kind of object responsible for the injury may be disclosed by the autopsy.

In attempting to reconstruct the circumstances in which a given injury was sustained, three possibilities should be borne in mind. The destructive effects of an impact may be limited to the site to which the force was applied, may be situated at a distance from it, or may be in part local and in part distant.

FRACTURE AT THE SITE OF IMPACT

Bone is generally more susceptible to fracture by traction than by compression. Thus, since the initial effect of an external impact against the head is usually to compress the outer table and stretch the inner table the latter is the first to fracture. If sufficient indentation occurs a fracture which began in the inner table will extend through to the outer. Obviously the formation of a single crack is not the only form taken by the local injury. It is by no means unusual to find several lines of fracture radiating from a point beneath the site of impact. The presence of multiple systems of intersection fissures usually indicates that multiple impacts have been sustained. The momentary deformity created by an impact may be so great that concentric lines of fracture develop around the central point so as to bring the radiating fissures into communication with one another. Such a lesion tends to reproduce the web-like pattern often seen in a shattered pane of glass.

Case 4.—A man was found dead of head injury on a cement parapet at the bottom of a 12-foot embankment. The fact that the decedent was known to have been drunk when last seen alive, and that there was no guard rail on the embankment, led to the assumption that his death had resulted from an accidental fall. The disclosure at autopsy, however, that there were three distinct systems of fissures in his skull indicated that the injuries had resulted from assault rather than from accident. It was apparent that the dead man had been struck twice on the left side and once on the right side of the head with a long, heavy cylindrical instrument, which was estimated to measure about one inch in diameter. Further police investigation led to the apprehension of the assailant. An iron pipe had been used in the attack.

MECHANISMS OF HEAD INJURY

Occasionally the force of an impact is expended locally, so as to depress a circumscribed plate of the outer table into the diploe. If the vertical supports of the diploe beneath the site of the impact are sturdy, the external table may remain intact but portions of the inner table may be dislodged in the form of one or more flakes.

Bullet wounds of the skull bear certain highly characteristic features. The passage of a bullet through a flat bone ordinarily results in the production of a cone-shaped defect, the diameter of which is greater on the side of exit than on the side of entrance. Thus, large chips of the internal table may be dislodged and driven against the brain despite the

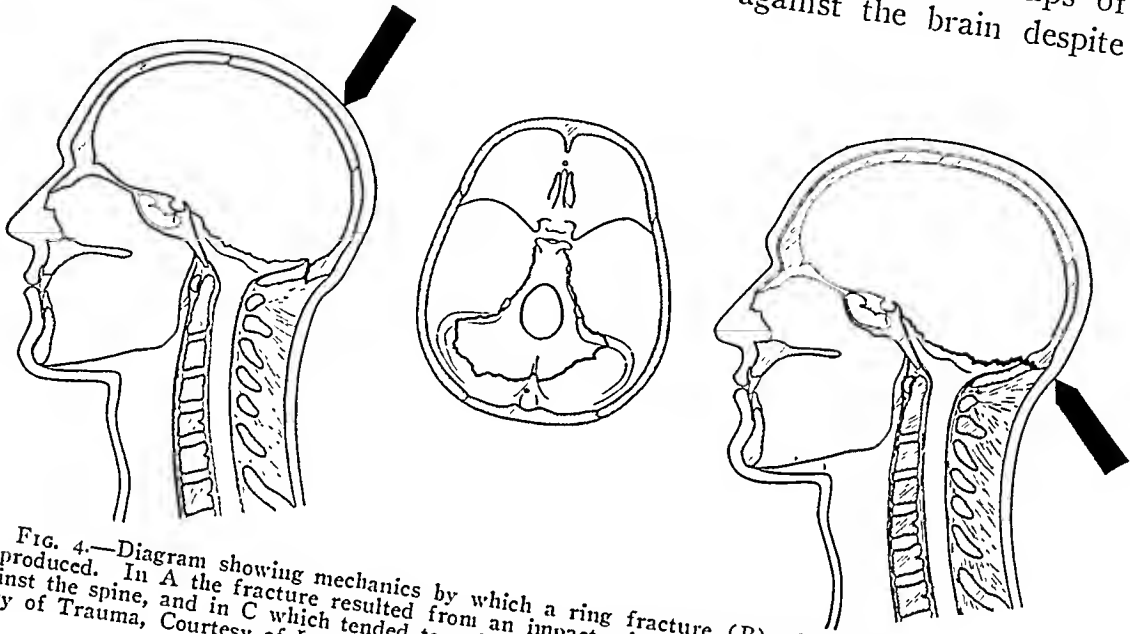


FIG. 4.—Diagram showing mechanics by which a ring fracture (B) of the base of the skull may be produced. In A the fracture resulted from an impact which tended to drive the base of the skull against the spine, and in C which tended to pull the skull away from the spine. (From Moritz, Pathology of Trauma, Courtesy of Lea & Febiger)

fact that the corresponding wound in the external table is small. Furthermore, the wound made by a bullet leaving the head is usually larger than the one produced where it entered. This is probably due to the fact that the bullet is often deformed or thrown off center by its first impact so that it presents a broader surface of impact when it strikes the bone on the opposite side. In the case of injuries by high velocity projectiles, fragmentation of a large part of the skull may result from the explosive effects of the collision.

Case 5.—Two small round defects were found in the skull of a badly charred body which was recovered from a burned dwelling. It was apparent to the pathologist that the defects had been produced by a bullet and that death had occurred prior to the conflagration. One of the holes was in the roof of the mouth and the other was in the top of the head. A gun, extensively damaged by the fire, was found near the body and it could not be determined whether it had been the property of the deceased or not. Obviously, the district attorney wished to know whether the death had resulted from suicide or homicide. The latter possibility was enhanced by the fact that the dead man was known to have kept a large sum of money on the premises. The contour of the wounds in the bone provided clear evidence that the bullet had entered the skull by way of the mouth and that the muzzle of the gun was probably

in contact with the palate when the fatal shot was fired. It was concluded, therefore, that death probably resulted from suicide rather than homicide.

When the muzzle of the gun is held in contact with the head at the moment of firing, rapidly expanding gases of combustion may enter the cranial cavity with the bullet. In such an event the entrance wound in skin and bone may be large and it is not unusual to find that a large part of the floor of the skull has been blown out. Such explosive basilar fractures are likely to have a butterfly pattern and may or may not communicate with the wounds of entrance or exit. Occasionally, despite the fact that a bullet has glanced off the skull without penetrating it, fragments of the internal table may be detached and driven against the brain with sufficient violence to produce severe cerebral damage.

FRACTURE DUE TO TRANSMITTED STRESS

As already indicated the destructive energy of blunt force is frequently transmitted in such a manner as to result in a fracture at a considerable distance from the site of external impact. The two most important factors in determining whether or not disruptive stresses will be transmitted to other parts of the skull are first, the elastic properties of bone at the site of impact and, second, the velocity of the impact. If the skull is relatively inelastic at the site of primary impact it will resist deformity and break locally at the moment when the distorting force exceeds the cohesiveness of the bone. If the bone at the site of impact is elastic and if the energy of impact is liberated slowly enough to overcome its local inertia, the skull will be deformed and fracture will occur at the site of greatest mechanical disadvantage.

The base of the skull is comprised of relatively heavy bones which tend to break rather than bend when subjected to deforming force, whereas the bones comprising the vault are thin and relatively elastic. The base is accordingly more vulnerable to fracture when subjected to a deforming force than is the vault. Thus, a frontal impact characteristically results in a fracture which begins at or near the site of injury and runs backward through the base of the anterior fossa. An impact against the side or back of the head characteristically results in fractures which run, respectively, inward through the middle or anteriorly through the posterior fossa.

Fractures of the base, also, result from forces which tend to drive the skull against or to tear it away from the spine. Thus, a blow on the top of the head or a fall on the buttocks may force the skull against the spine with sufficient violence to break a circular or ovoid plate out of the floor of the skull around the foramen magnum. Similarly, the upward thrust of an impact from below against the back of the head may exert sufficient shearing stress at the craniospinal articulation to produce a circular fracture of the base. Such a fracture may encircle or communicate with the foramen

magnum. If the lateral limbs extend forward through the petrous portions of the temporal bones they are likely to communicate with each other in or behind the sella to complete the circular fracture anteriorly.

INJURIES OF THE INTRACRANIAL MEMBRANES AND THEIR VESSELS

A blunt impact to the head may injure the dura, the dura and leptomeninges or only the leptomeninges.

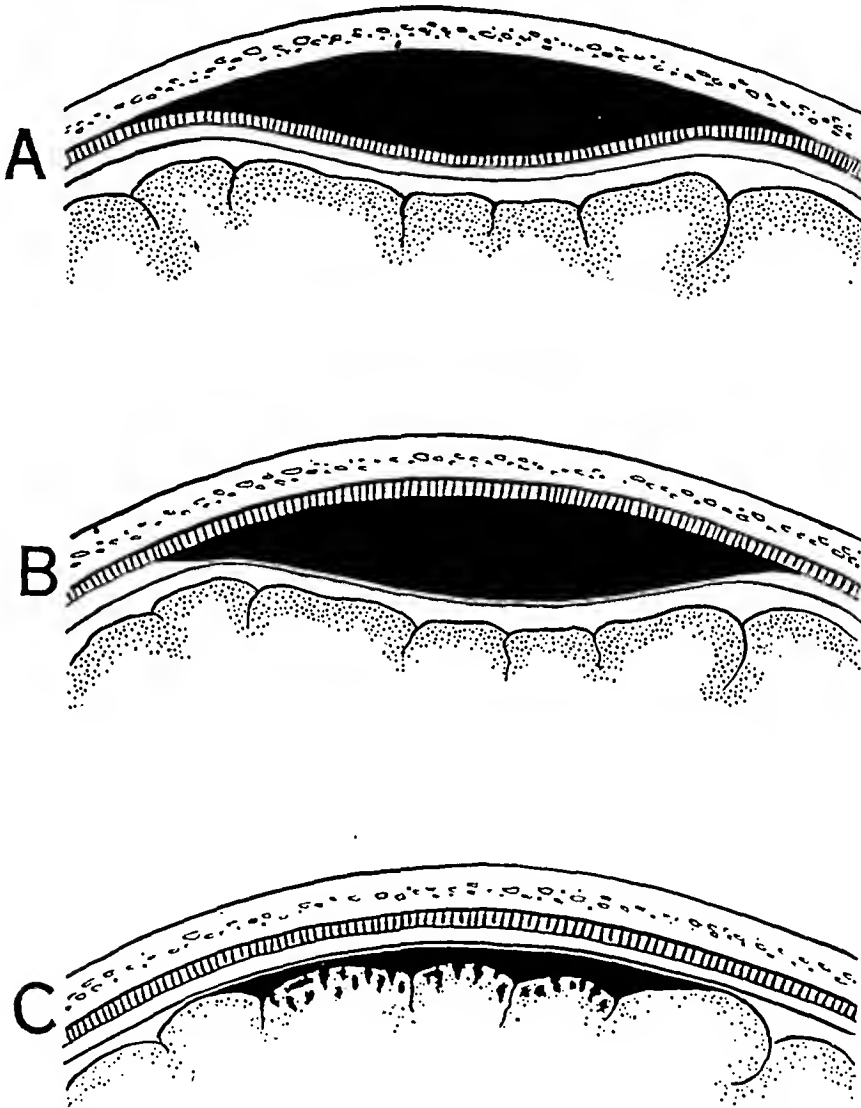


FIG. 5.—Common Sites of Posttraumatic Intracranial Hemorrhage: A. Epidural. Usually with fracture and beneath site of impact. B. Subdural. With or without fracture. May or may not occur at site of impact. C. Subarachnoid with superficial cerebral injury. With or without fracture. May occur at site of impact, at opposite pole of brain, or in both situations.

As already indicated, the dura is lacerated whenever the separation of the edges of the fractured bone exceeds the elasticity of that membrane. A defect in the dura is not in itself important except as it may create a portal of entry for infection, be associated with hemorrhage or predispose to the formation of adhesions between skull and brain. Dural defects in the vault or in the posterior fossa do not ordinarily predispose to infection. Defects

in the base, however, may lead to a direct communication between the pia-arachnoid and the middle ear, the accessory air sinuses or the nose.

Two sites of dural injury are of particular importance in relation to intracranial bleeding. One is in the vicinity of the great venous sinuses and the other along the course of the middle meningeal artery. Laceration of the former may lead to the rapid accumulation of a massive subdural hematoma and laceration of the latter often results in the formation of a rapidly fatal epi- or subdural hematoma.

It should be borne in mind that traumatic subdural bleeding frequently occurs without coexistent damage to the dura itself. A blunt impact, even though the skull remains intact, may cause sufficient agitation of the intracranial structures to lacerate the small veins that bridge the subdural space. Such vessels are most numerous in the vicinity of the sagittal sinus and beneath the under surface of the temporal lobes.

Case 6.—An elderly man, living alone in a rooming house, was found dead in bed one morning. He had been heard to enter his room at about 11:00 P.M. on the preceding evening and had appeared to be in his usual good health when last seen alive at 7:00 P.M. His door was locked from the inside, and there was a telephone on his bedside table. There was no external evidence of injury and it was assumed that the decedent had suffered a heart attack during the night. Since, however, there was no available history of previous heart trouble it was decided to perform an autopsy.

Postmortem examination disclosed a theretofore unsuspected bruise on the back of the head and a large recent subdural hematoma over the right hemisphere. Police investigation of the movements of the deceased during the evening prior to his death revealed that he had fallen while ascending the steps of a friend's house. According to the friend, he had been stunned a few moments but recovered sufficiently to play a game of cards. At about 10:00 P.M. he complained of a headache of increasing severity and had gone home.

It was apparent from the medical evidence that death had resulted from violence rather than from natural causes. The existence of a considerable amount of accident insurance made this finding a matter of practical rather than academic interest.

Old persons and chronic alcoholics are particularly susceptible to head injury, and subdural hemorrhage may follow impacts so mild that little or no immediate attention is paid to their occurrence. The bleeding is often so slow that days or even weeks elapse before its occurrence is recognized.

If, as is sometimes the case, the arachnoid is also torn, cerebrospinal fluid may escape into the subdural space and mix with the blood. Obviously, in such circumstances, there will also be an escape of blood into the cerebrospinal fluid.

The leptomeninges are likely to be damaged concomitantly with the dura if the latter is lacerated, and concomitantly with the cerebral cortex if the brain is severely bruised or lacerated. If both the dura and the arachnoid are lacerated at the same site cerebrospinal fluid is free to escape into the extracranial tissues or spaces. When such defects communicate with the nose, ears, or accessory air sinuses, leptomeningitis is likely to result.

MECHANISMS OF HEAD INJURY

If the arachnoid remains intact posttraumatic adhesions do not form between brain and dura. If, however, the arachnoid and dura are interrupted at the same site dense fibrous adhesions are likely to form. Such adhesions are strongly epileptogenic.

Laceration of cortex as it is pulled away from the decelerated skull.

Contusion of cortex as it receives the backward thrust of the decelerated skull.

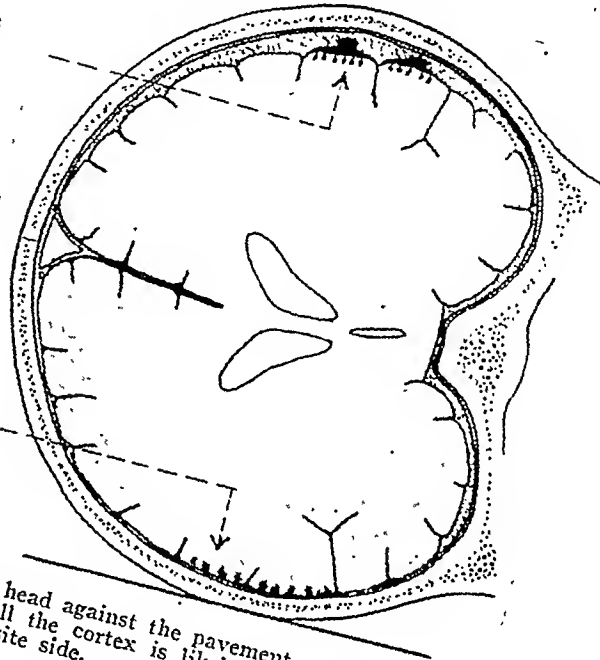


FIG. 6.—Impact of rapidly moving head against the pavement. Since the brain is decelerated less rapidly than the skull the cortex is likely to be bruised on the side of impact and lacerated on the opposite side.

CONCUSSION OF THE BRAIN

The phenomenon of being stunned or rendered temporarily unconscious by a blow on the head depends for its occurrence on a sudden change in the state of rest or motion of the head. If at the moment the head is struck it is supported in such a manner that it remains stationary, extensive injury to the brain may be sustained without loss of consciousness. However, if the motionless head is suddenly accelerated or if the rapidly moving head is suddenly decelerated concussion is likely to result. Recent experimental observations¹ have failed to disclose any characteristic morphologic changes in the suddenly decelerated concussed or if the rapidly moving head is suddenly decelerated concussion is likely to result. Contrary to opinions held in the past, the sudden rise in intracranial pressure caused by external impact does not appear to be responsible for the phenomenon, nor does it appear to depend on the occurrence of cerebral ischemia due to reflex vascular spasm. Obviously, the occurrence of a concussive injury does not exclude the possibility of other forms of cerebral damage. By the same token, posttraumatic unconsciousness is not invariably the result of concussion. Although a fall to the pavement may result in such rapid deceleration of the moving head as to cause loss of consciousness, the same impact may result in cerebral damage so severe as to account for unconsciousness independently of concussion. Even though concussion is not sustained the progressive elevation of intracranial pressure due to hemorrhage from damaged

blood vessels may cause unconsciousness. The latent period between injury and loss of consciousness from hemorrhage may be seconds, minutes, or many hours, depending upon the rapidity of the bleeding. An individual who is "knocked out" by a fall and who regains consciousness after a few minutes, only to lose it again after a few hours because of intracranial bleeding, constitutes a good example of both "concussive" and "nonconcussive" unconsciousness.

CEREBRAL INJURIES BY BLUNT VIOLENCE

The impact of skull against brain beneath the site to which external force is applied may result in contusion, laceration, or crushing of the underlying cortex. The force may be sufficient to destroy a large part of a lobe, or it may be expended in the production of a shallow bruise of the eminences of one or two of the subjacent convolutions. After either bruising or laceration localized ischemia induced by the interruption of small blood vessels may result in secondary enlargement of a lesion. The contraction of scar tissue at the site of a cerebral injury may result in the development of functional disturbances from a theretofore silent lesion.

Neither contusion nor laceration is necessarily limited to, nor do they necessarily occur in continuity with the site of external impact. If the impact is sufficiently severe the brain may be displaced so as to collide with a fold in the dura with sufficient violence to cause laceration. Thus, the corpus callosum may be torn by being thrust against the falx cerebri or the peduncles may be lacerated by collision with the tentorium. When such lesions are produced, other more severe injuries to the brain are usually sustained.

The mechanism by which *contrecoup* injuries of the cortex are produced is not always clear. The impact of a moving head against a stationary object frequently results in cortical damage on the side opposite that which sustained the external impact. Thus, a fall on the back of the head frequently results in the production of more extensive cortical injury to the frontal than it does to the occipital lobes. Similarly, it is not unusual for a blow over the left hemisphere to result in damage to the right or for a blow over the frontal region to cause injury of the occipital lobes. Occasionally contralateral injury results from an impact which neither sets the head in motion nor brings the moving head to a stop. In such an event the contralateral lesion is most plausibly explained on a basis of contusion. The skull is compressed bilaterally and the brain is squeezed between the inwardly moving sides.

In most instances contusion fails to provide a satisfactory explanation for *contrecoup* injury because the nature of the trauma is such that the occurrence of a contralateral impact between skull and brain is extremely unlikely. The most common type of injury to result in a *contrecoup* lesion of the cortex is a fall in which the rapidly moving head strikes a resistant object. In such an event, the forward momentum of the brain will tend

to tear it away from the side of the skull opposite the point of impact, and the traction thus exerted on the arachnoidal trabeculae leads to laceration of the underlying brain substance.

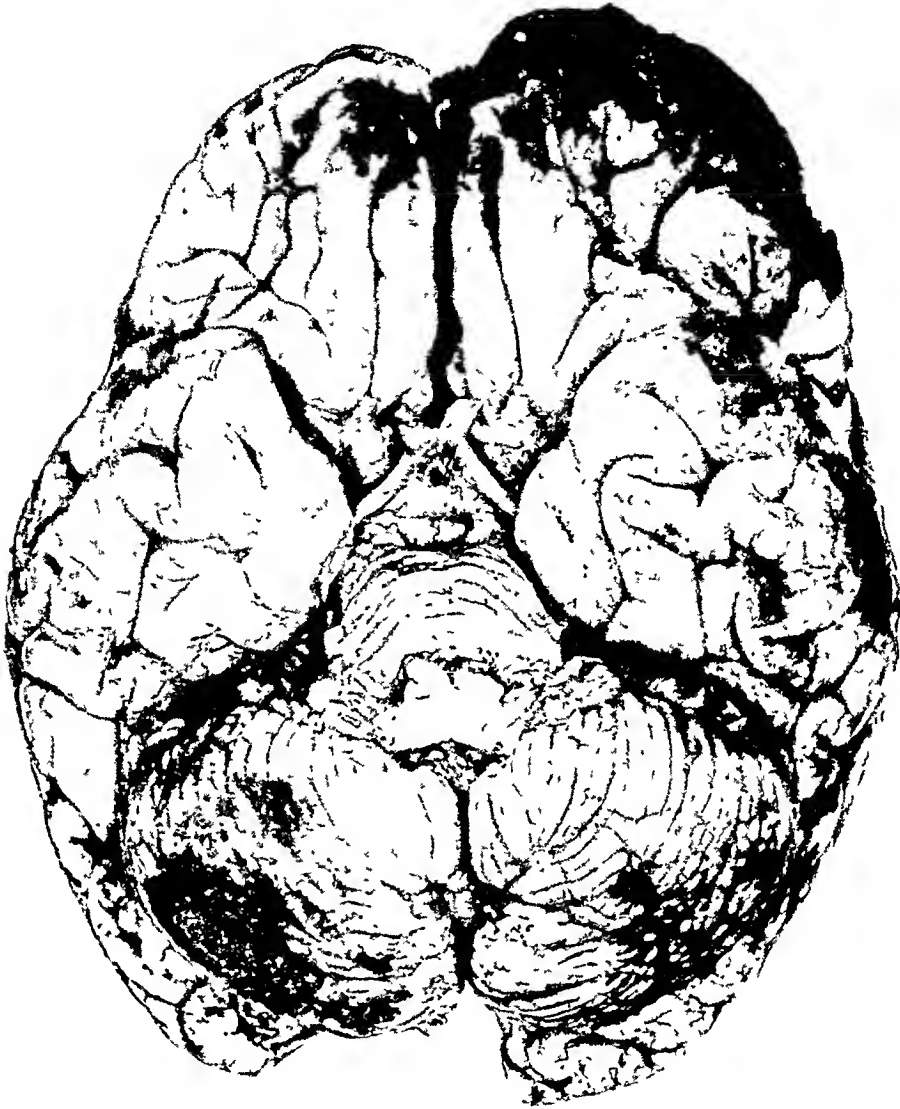


FIG. 7.—Photograph of the under surface of a brain showing the effect of direct and *contrecoup* injury. The external impact was sustained on the right side of the back of the head. The direct effect of the blow is seen on the surface of the right lobe of the cerebellum and the *contrecoup* injuries are most pronounced at the anterior pole of the left frontal lobe.

DIFFUSE CEREBRAL INJURY BY BLUNT IMPACT

The mechanism by which blunt impact produces diffuse in contrast to local injuries of the brain is often obscure. Whereas superficial bruising and laceration can be attributed to compression or traction, no such simple explanation suffices to account for the widely disseminated internal lesions that are occasionally sustained. Such lesions usually take the form of multiple petechiae or scattered foci of degeneration and necrosis. That they are probably caused by agitation of the brain as a whole is indicated by the fact that they are sometimes observed independently of a recognizable cortical

lesion. Disseminated foci of progressive gliosis following nonpenetrating injuries of the head probably have their origin in such lesions.

PENETRATING INJURIES

There is little to be said regarding the mechanism of injury incident to penetration of the brain other than to call attention to some of the special characteristics of wounds produced by bullets. Regardless of the size, shape or velocity of a bullet, when it strikes the skull with sufficient force to penetrate, it usually produces a larger defect where it emerges from the inner table than where it enters the external table. In doing so multiple fragments of bone, each constituting a secondary missile, may be driven into the cortex in the vicinity of the tract of the bullet.



FIG. 8.—Photograph showing the forward and lateral thrust imparted by a bullet in its passage through clay. It is to be noted that the diameter of the resulting defect is much greater than that of the bullet. The muzzle of the gun was approximately 18 inches from the target at the moment of firing.

Frequently the bullet is thrown off center as a result of its impact against bone so that its wobbling produces a larger defect in the brain than would be expected from the diameter of the projectile. Whether it wobbles or not a bullet imparts a lateral and forward thrust to the medium through which it passes, the result of which is the production of a broad cylindrical- or spindle-shaped defect in a tissue as soft as the brain. High velocity bullets such as are fired from military weapons and from certain sporting rifles are likely to disintegrate into many fragments as they pass through the body. Each such fragment becomes a secondary missile and contributes to the total effect of the injury.

SUMMARY AND CONCLUSIONS

It has been attempted in the foregoing discussion to relate some of the more common traumatic lesions of the scalp, skull, meninges, and brain to the kinds of mechanical disturbance responsible for their production.

From a medicolegal standpoint, it is important not only to know the kind of lesion that may be regarded as the natural consequence of a given type of injury, but also to be able to reconstruct the probable circumstances of an unwitnessed injury from the character and location of the anatomic lesions.

Mechanical injuries of the head have been classified as penetrating and nonpenetrating. The principal differences between penetrating and non-

MECHANISMS OF HEAD INJURY

penetrating head injuries lie in the fact that the former are more frequently associated with the presence of intracranial infection, ordinarily involve greater primary destruction of brain tissue, and are more frequently followed by the formation of craniocerebral and intracerebral scars.

The immediate loss of consciousness following injury of the head may be due either to a sudden agitation of the head, with or without the production of recognizable morphologic changes, or to direct mechanical disruption of brain tissue independently of agitation of the head as a whole. Delayed onset of unconsciousness or nonrecovery from immediate posttraumatic unconsciousness usually indicates the occurrence of intracranial bleeding, with an associated increase in intracranial pressure. Such bleeding may be epidural, subdural, subarachnoid, or intracerebral. Other sequelae of mechanical injury which may be responsible for delay in the onset or prolongation of the duration of unconsciousness include secondary cerebral vascular disturbances, edema, and infection.

Residual posttraumatic disability after apparent recovery from a head injury may be due to the contraction of craniocerebral adhesions or intracerebral scars, to secondary cerebral circulatory disturbances, to the presence of intracranial foreign bodies, to the presence of intracranial infection, or to obscure causes not associated with recognizable gross or microscopic abnormality.

REFERENCE

- ¹ Denny-Brown, D., and Ritchie Russel, W.: Experimental Cerebral Concussion. *Brain*, 64, 93, 1941.

FORENSIC ASPECTS OF BURNS

SPECIAL REFERENCE TO APPRAISAL OF TERMINAL DISABILITY

ROBERT HENRY ALDRICH, M.D.

BOSTON, MASS.

THE BURNED PATIENT presents a great many problems that concern the lawyer as well as the doctor. The immediate problem of saving life and restoring the burned individual to society is the primary care of the physician, but, unfortunately, the final outcome frequently is complicated by factors producing results that are far from perfect. These factors are of interest to the lawyer who is attempting to determine the proper methods for evaluating legal settlements. It is true that the lawyer can turn to the medical profession for aid, but he himself should know something of the fundamentals presented by the burned patient to enable him to move more quickly, and more justly, complete his work.

In peace-time burns occur all too frequently. According to statistics published by the National Safety Council in 1940 and 1941, burns killed 23 per cent of all children under the age of five who died from accidental means. From age 5-15, burns killed 13 per cent of all those dying violent deaths, and from 15 years on burns took a yearly toll of six per cent of all victims exterminated by accidents. There are no statistics to indicate the number of people who received burns but lived. However, from the figures obtained at the Boston City Hospital, where there is a very large burn population, it is evident that about 1000 patients receive burns and live, for the one who is burned and dies. Approximately ten per cent of those that live are badly enough burned to be hospitalized. It is in this group that the many problems of interest to the lawyer occur.

There are a number of angles which have to be studied by the lawyer to arrive at his final decision. Most of these can be estimated if he knows the cost of medical care, the time-element involved, the immediate disability after healing is complete, and the probabilities and possibilities regarding future pathology.

DEFINITION OF A BURN

A burn is a loss of continuity of the body surface due to a coagulation and destruction of skin and subcutaneous tissues by thermal changes, including both heat and cold, by chemicals, by electricity, and by radiation. No distinction should be made between a burn and a scald, inasmuch as they are pathologically the same, and must be considered identical from the viewpoint of physiology and treatment.

CLASSIFICATION

The classification of burns refers to the depth of the pathology or to the amount of tissue involved. In the past, the classification of Dupuytren was

FORENSIC ASPECTS OF BURNS

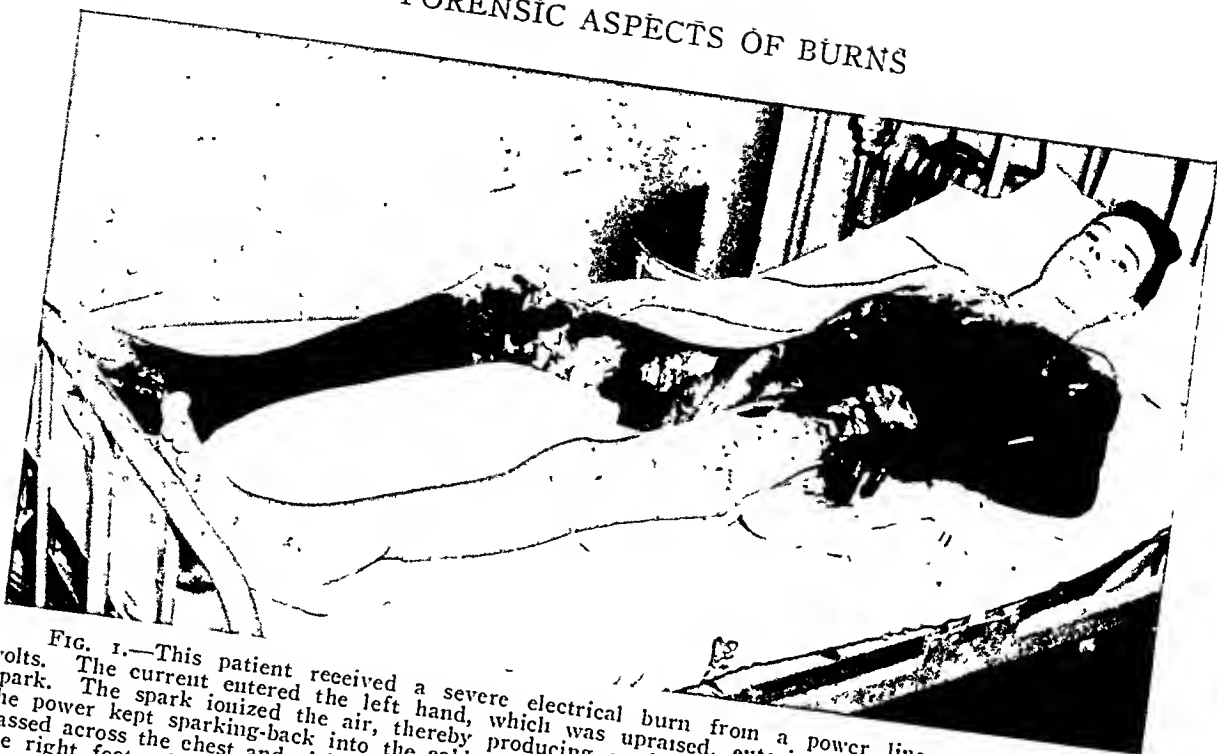


FIG. 1.—This patient received a severe electrical burn from a power line containing 33,000 volts. The current entered the left hand, which was upraised, entering the palm and fingers as a spark. The spark ionized the air, thereby producing conductivity to the rest of the arm. Most of the power kept sparking-back into the cable from the left arm, but enough current remained, which passed across the chest and abdomen and down the right leg, to ground itself on a steel girder beneath the right foot. The heat was so intense that it set the clothing on fire. The patient was immediately knocked to the ground and did not breathe for three hours and ten minutes. He was kept alive by artificial respiration. After treatment for shock he received the aniline dye treatment on the burns. His convalescence was quite stormy due to many complications. He had an amnesia for two weeks after the burn took place. There was injury to the left kidney due both to infection and to the electrical current passing through the kidney area. The left arm was almost completely cooked, and at many times it was considered advisable to remove the arm. However, as this procedure is irreversible, the arm was left on. It can always be removed in the future if it gives him further trouble. The patient had special nurses for four months, and had six months of hospitalization. He had repeated transfusions and skin grafting was necessary on the left arm. The final result was excellent both from the cosmetic and functional points of view except for the left arm.

In the final award on the case the sum paid was based on the expense of the medical care and the suffering the patient underwent. The factors of later terminal disabilities were taken into consideration. The possibility of cancer was considered, and it was also brought out that the left kidney was probably partially damaged, and that sterility would probably result. The two weeks of amnesia following the burn indicated brain damage, and this was also an element in the verdict.

The patient in this case brought suit against both the power house where he was making a survey and the technical school that he was attending. Electrical experts established the fact that the power box on the wall, which was the source of the current that injured the boy, was not marked as being dangerous and was placed too close to the floor.

Medical testimony was introduced to show the extent of the injury and the probabilities and possibilities of future disabilities. The judge gave a verdict against the power house of \$15,000. \$5,000 was paid for hospitalization, nursing and medical care. The actual bills amounted to this sum. The additional \$10,000 was allowed to compensate for the suffering the patient went through, and to allow him to complete his education for rehabilitation in society. It was recognized that the left arm was useless, and that future complications may prevent the patient from earning his own living for some years.

This award is still held in escrow until the case has been brought against the technical school.

advocated. This listed seven degrees, and was quite confusing. A much simpler form of classification has been adopted in which the burns are divided into three degrees. A first degree burn is one in which there is simply an erythema of the area involved. An example of this is the common sunburn. A second degree burn indicates a destruction of the epidermis. This is roughly the outer half of the skin. In this type of burn there is usually blister formation due to the exudation of plasma from the deeper layer of the epithelium which elevates the epidermis. A third degree burn indicates involvement of the full-thickness of the skin and any of the subcutaneous tissues. When the deeper structures are involved there is no change in the classification, the burn still being referred to as a third degree one.

THE PATHOLOGY

When a burn is produced by thermal changes and chemicals there is immediate destruction of the tissues involved in the local area. The destruction is one of coagulation, the living cells are converted into necrotic tissue, the blood and nerve supply to them are interrupted, and they become a foreign body to the host. Shortly after this occurs there is a dilatation of the capillary blood vessels around the burned area. Those capillaries near the site of the burn undergo a change in the permeability and allow plasma to escape into the interstitial spaces. This escape of plasma compresses the return flow of lymph. Outside of the area of local edema there forms the so-called pyogenic membrane, which consists of a thin wall of round cells. These leukocytes act as a defense mechanism to prevent invasion of the body by germs. The edema of the burned part usually reaches its peak in 12-18 hours, and remains for a period of three to seven days. At the end of that time there is reabsorption of the lymph and repair processes begin to set in. The exact nature of these depends entirely upon the site of the burn, its size, and the general condition of the patient.

Burns of roentgenray origin and electrical burns are apt to be slower in manifestation and much more extensive due to the penetration of the electrical energy. The destruction of tissue, however, is just as concrete and involves the body in the problem of repair.

SHOCK

Burn shock is a manifestation of symptoms and physical signs seen in practically all large burns. The mechanism of shock is still not completely understood. It is known that in shock, whatever may be its origin, there is a certain specific syndrome. This consists of a fall in blood pressure, associated with a decreased coronary output, a change in the capillary permeability on the body as a whole, releasing plasma from the blood stream into interstitial spaces, and a general depletion of all of the vital functions due to anoxemia, lowered venous pressure and a depletion of the circulation.

In most major burns the factor of shock is the immediate problem, and must be combated with heat, rest, the control of pain, and intravenous replacement therapy if the patient is to survive. The amount of shock depends on the size of the burn, the part of the body burned and, to a certain extent, with the speed in which the burn takes place. It is conservative to state that at least 75 per cent of the deaths that occur in the first 72 hours following the inception of the burn are due to shock.

INFLUENCE OF SIZE OF BURN ON DISABILITY AND LIFE

Burns can be divided into the classification of major and minor, depending on the surface area involved: Empirically, a minor burn is one in which less than 15 per cent of the body surface is destroyed. A major burn is one in which there is involvement of more than 15 per cent. This may seem, at first, to be a didactic classification, but it is essential when it is realized

FORENSIC ASPECTS OF BURNS

that minor burns usually need only local treatment with no thought of shock, whereas the major burns invariably need shock therapy as well as treatment to the local areas. There is a limit to the amount of body surface that can be burned without producing death. Until recently a burn of more than one-third of the body was considered fatal. At the present, because of advancement made in local treatment and the use of intravenous plasma, it is now possible to save burns that involve up to 65 to 70 per cent of the body area. It is obvious that the larger the burn, the more profound the shock, and that the incidence of disabilities increase in direct proportion to the area involved.

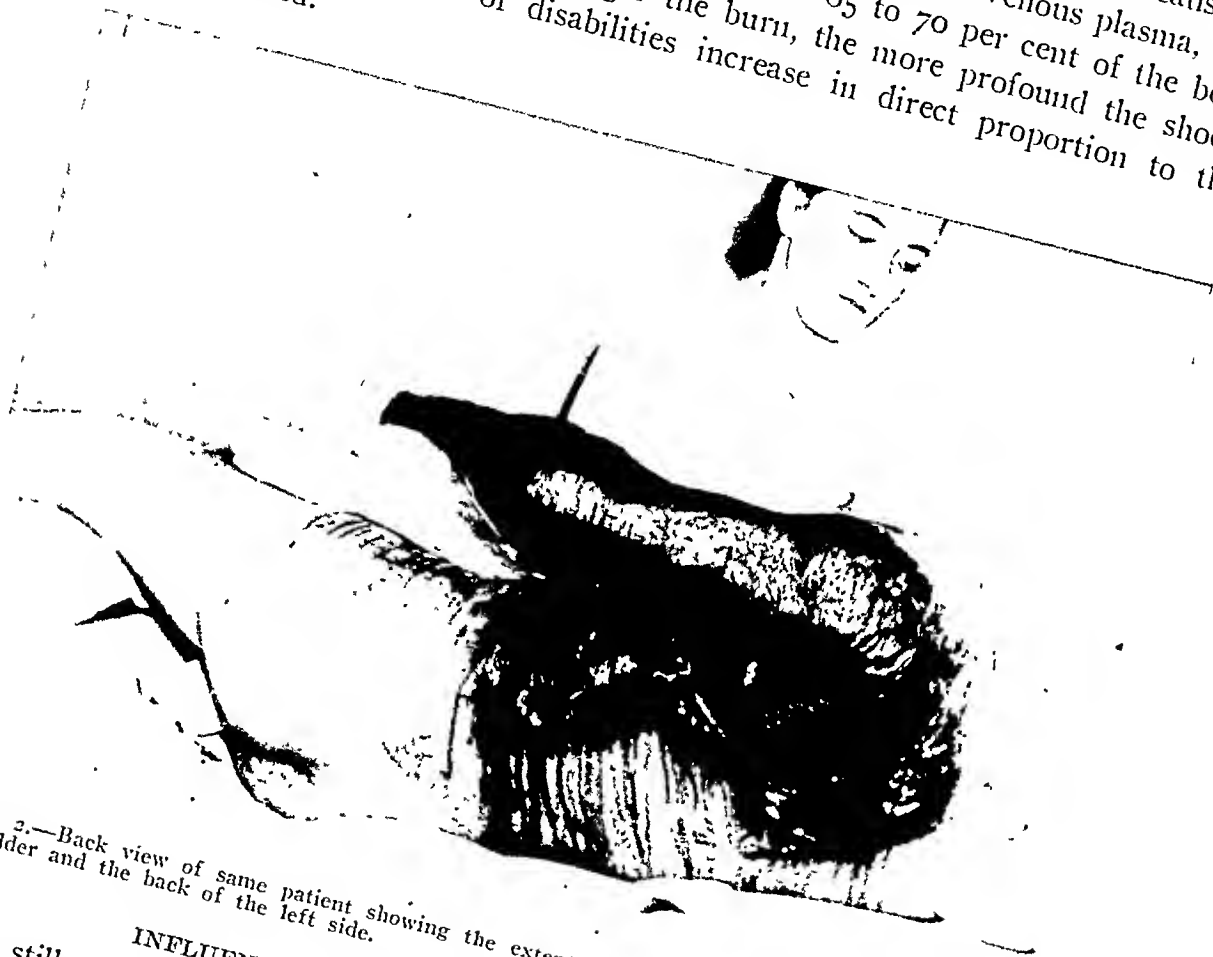


FIG. 2.—Back view of same patient showing the extent of burn on the posterior aspect of the left shoulder and the back of the left side.

INFLUENCE OF AGE ON DISABILITY AND LIFE

It is still debatable as to what factor age plays in the recovery of the burned patient and in his disability if he does recover. In general, it can be stated that very young children have little reserve strength to combat their pathology. Older children and young adults can withstand a tremendous amount of trauma and apparently have much better powers of healing. Corrective measures such as plastic surgery are more successful in children than in adults.

RESTORATION AND HEALING OF THE THREE DEGREES OF BURNS

In order to understand the complications and disabilities that may result from a burn, it is essential to understand some of the fundamentals of the repair processes. Nature attempts to restore the body to its original pattern,

but the end-result is not always ideal. The factor of the depth of the burn has a large bearing on what the final outcome will be and the disabilities that may result.

A first degree burn heals by a return of the erythema to the normal circulation and by desquamation. The hornified layer of the epithelium peels or flakes away over a period of a few days. The underlying skin builds up a new hornified layer. This is done with no scarring and with no real disability except that caused by pain or by the systemic reaction which is usually present for only 24 to 48 hours. The systemic reaction probably results from both pain and the action of the actinic rays on the body. There can be no absorption of a poisonous protein, and there can be no infection as there is no portal of entry caused by a break in the skin. In severe sunburns, heat prostration or sunstroke may occur.

Second degree burns heal by building up an intact skin from the dermis. The epithelial cells composing the dermis have to undergo a change in character to assume the rôle of the epidermis. The fact that the floor of the burn is paved with epithelium results in fairly rapid healing with little, if any, permanent disability or deformity. Second degree burns are apt to be more painful than the third degree type because the nerve endings in the skin have not been killed, but have been exposed. This increase in pain is apt to produce a greater degree of shock. The dermis has little immunity to infection, and may allow a severe infectious toxemia to occur. If second degree burns are cared for properly and the dermis is not killed by infection or by harsh local treatments, there is never need for skin grafting, and the cosmetic and functional result will be almost perfect.

Third degree burns heal in one of two ways, depending upon the depth of the burn. If only the full-thickness of the skin is destroyed healing will eventually occur by the spread of the islands of epithelium that are beneath the skin at the bases of the hair follicles and sweat glands. These islands will eventually come to the surface of the granulating wound and will spread and coalesce, giving a scar that is quite thin and flexible. This scar, while it is not always ideal in appearance, usually does not disturb the function of the part involved. When the burn involves the entire skin and the underlying tissues, healing can only progress from the edges of the wound or from skin transplanted from other parts of the body. This is the type of burn that gives rise to severe contractures and deformities if too long a time-element elapses before the burned surface is covered. In the granulation tissue that builds up in the burned areas contracture bands are formed from fibroblastic cells. These contracture bands can be very dense and can produce many untoward results.

IMMEDIATE DISABILITY FOLLOWING A BURN

The immediate disability following a burn consists of shock and toxemia. The shock occurs very shortly after the burn takes place and may last from only an hour or two up to a week or ten days, depending on the size of the burn and the treatment instituted. The toxic phase, due to infection, begins

FORENSIC ASPECTS OF BURNS

about 40 hours after the burn takes place and may persist until healing is almost complete. In severe burns this may be for four or five months, or even longer. There is also the emotional factor to be considered. It is usually the active healthy child or the well individual who gets burned. The rapid transition from being perfectly well to a bedridden patient reacts strongly on a large percentage of the stricken individuals. They are usually frightened, apprehensive of death, and they worry a great deal about their being restored as normal individuals. The adult male is prone to wonder about his ability to support himself and others, and the female is inclined to become very depressed regarding her final appearance.



FIG. 3.—View of foot showing where the current arced from the foot into a steel girder.

IMMEDIATE DISABILITY FOLLOWING THE HEALING OF THE BURN

The disability following the healing of the burn is due to a number of factors. The more common ones are disabilities due to scar formation, to the development of keloid, to contractures in general, to lowered resistance to other diseases, to psychic trauma, to the development of unwanted emotional complexes, to inability to assume former rôles in society, and the loss of strength and activity. These factors are all perfectly obvious and self-explanatory and need not to be gone into fully. All of these factors, however, are very definite and must be considered in trying to evaluate the terminal disability of the burned patient.

LATE DISABILITIES FOLLOWING HEALING

Some of the disabilities listed above may put in their appearance many weeks or months after the burn has apparently healed. It is possible for

contractures and keloid formation to occur in burns that are fairly old. If such contractures interfere with the movements of the body, it is impossible for the individual to assume all of his former functions and duties. Frequently, contractures can occur around orifices of the body preventing or interfering with the natural functions such as defecation, urination, sexual intercourse, and even eating. Late disabilities are prone to produce a lack of social adjustment, thus having a direct bearing on the emotional stability of the patient.

COMPLICATIONS AND MORBIDITY

When a patient has undergone a long period of convalescence characterized by a profound state of shock in the beginning and many months of infectious toxemia, many organs of the body become injured beyond repair even though they are far removed from the site of the burn. Renal complications, such as nephritis, may have a permanent influence on the general health of the patient and his life expectancy. Prolonged infection can also injure the heart and may force the patient into a sedentary life. Electrical burns may cause permanent nerve or brain injury and may have a bearing on the sexual development and the sex life of the patient if the current involves the gonads. It is also a well-established fact that skin cancer is much more prone to develop in the scars produced by burns than in normal skin. All of these complications must be considered in evaluating the possible or the probable end-result the patient may expect.

THE COST OF BURNS

Because burns result in such profound and immediate disability, they are apt to be exceedingly costly to the individual or to the institution caring for the individual. All patients with large burns need very special care and constant attention. From the medical aspect large burns must be seen by the physician at least once a day and in extreme cases three and four times a day. These burns need trained nurses in constant attendance. Frequently, consultations with specialists must be obtained to determine plans of treatment. The treatment itself consisting, as it does, of large quantities of plasma, special diets and expensive vitamins, is not a cheap one. After the patient is healed he may have to undergo extensive plastic operations, involving more hospitalization and lost time from productive work. Burns of one-fourth of the body area, or more, produce absenteeism from employment for weeks and months. This loss of production has to be counted in as a part of the cost produced by the burn.

ESTIMATION OF THE DISABILITY AS A WHOLE

The estimation of the final terminal disability is a composite picture. The lawyer or the doctor, or both, must take into consideration all of the factors that were present from the time the burn took place, and sometimes it is necessary to go back many years before that. In general, it is considered

FORENSIC ASPECTS OF BURNS

that there are ten chief factors or fundamentals that have to be considered. They are:

- (1) Degree of the burn.
- (2) Size of the burn.
- (3) Part of the body involved.



FIG. 4.—Posterior view following healing.

FIG. 5.—Front view of patient after healing. Note the minimum scarring of abdomen, chest and right leg. The left arm is withered and is almost a total disability.

- (4) Age.
- (5) Physical condition of the patient before the burn took place.
- (6) Sex of the patient.
- (7) Amount of terminal disability produced by the burn.
- (8) Amount of psychic trauma produced by the burn.
- (9) Occupation of the patient.
- (10) The probabilities and possibilities of future morbidity.

These factors are quite obvious. It would require too much space to go into a complete discussion of each one of the above ten headings. It should be obvious, however, that, in most burns, the majority of disability and the proper settlement to be made must be based on some such schedule.

REFERENCES

- Aldrich, R. H.: The Rôle of Infection in Burns with Special Reference to Gentian Violet. *N. E. J. Med.*, 208, 299-307, February, 1933.

- Bardeen, C. R.: A Study of the Visceral Changes in Extensive Superficial Burns. *J. Exper. Med.*, N. Y., 2, 501-514, 1897.
- Berkow, S. G.: Ectropion of Lower Eyelid: Early Sign. *J. A. M. A.*, 90, 1708-1709, May 26, 1928.
- Berkow, S. G.: Value of Surface-area Proportions in the Prognosis of Cutaneous Burns and Scalds. *Am. J. Surg.*, 11, 315, February, 1931.
- Bettman, A. G.: Tannic Acid and Silver Nitrate in Burns. *Surg., Gynec. and Obst.*, 62, 458-463, February, 1936.
- Black, D. A. K.: Treatment of Burn Shock with Plasma and Serum. *Brit., M. J.*, 2, 693-697, 1940.
- Blalock, A.: Principles of Surgical Care: Shock and other Problems. St. Louis: C. V. Mosby Co.; 1940.
- Cumin, W.: Cases of Severe Burn: With Dissections, and Remarks. *Edinburgh Med. and Surg. J.*, 19, 337, 1823.
- Davidson, E. C.: Prevention of Toxemia of Burns. Treatment by Tannic Acid Solution. *Am. J. Surg.*, 40, 114-116, May, 1926.
- Davis and Kitlowski: Treatment of Old, Unhealed Burns. *ANNALS OF SURGERY*, 97, 648-669, May, 1933.
- Graham, E. A.: Yearbook of General Surgery. Chicago: Yearbook Publishers, 1939.
- Greenwald, H. M., and Eliasberg, H.: The Pathogenesis of Death from Burns. *Am. J. Med. Sc.*, 171, 682, 1926.
- Harkins, H. N.: Recent Advances in the Study of Burns. *Surgery*, 3, 430-465, 1938; *idem*: Treatment of Burns: Springfield, Illinois, 1941. Charles C. Thomas, in press.
- Lavender, H. J.: Burns and Their Treatment. *J. Med.*, 11, 635, February, 1931.
- Locke, E. A.: A Report of the Blood Examination in Ten Cases of Severe Burns of the Skin. *Boston M. & S. J.*, 147, 480, October 30, 1902.
- Lustgarten, S.: Zur Theorie der primären Todesursache bei Verbrennungen. *Wien, klin. Wchnschr.*, 4, 528, 1891.
- Moes, W.: Curlings Ulcer: Duodenal Ulcer Following Superficial Burns. *Am. Surg.*, 91, 527-532, April, 1930.
- Moon, V. H.: Shock and Related Capillary Phenomena. New York: Oxford Univ. Press, 1938.
- Naffziger, H. C.: *Surg., Gynec. and Obst.*, 70, 374, 1940.
- Pack, G. T., and Davis, A. H.: Burns. Philadelphia, J. B. Lippincott Co., 1930.
- Penberthy, G. C., and Weller, C. N.: Treatment of Burns. *Am. J. Surg.*, 46, 468-476, 1939.
- Penick, R. J., Jr.: Treatment of Burns: With Especial Reference to Use of Gentian Violet. *Internat. Clin.*, 1, 31-42, March, 1933.
- Robertson, B., and Boyd, G. L.: The Toxemia of Severe Superficial Burns. *J. Lab. and Clin. Med.*, 9, 1, October, 1923.
- Ronchese, F.: Duodenal Ulcer After Burns. *Reforma Medica*, Naples, 40, 753-755, August 11, 1924; *Obst. J. A. M. A.*, 83, 1038, September 27, 1924.
- Schall, J. H.: Antiseptic Treatment of Burns. *N. Y. M. Times*, 24, 265, 1896.
- Scudder, J.: Shock: Blood Studies as a Guide to Therapy. Philadelphia. J. B. Lippincott Co., 1940.
- Talmey, B. S.: Open Air Treatment for Burns. *N. Y. Med. J.*, 99, 558, 1914.
- Thiery, Paul: Des Applications de l'acide pierique a la therapeutique des brulures: Reratogenise et Reratoplastie. *Gaz. d. hop. Paris*, 69, 69-78, 1896.
- Underhill, F. P., Carrington, G. L., *et al.*: Blood Concentration Changes in Extensive Superficial Burns: Their Significance for Systemic Treatment. *Arch. Int. Med.*, 32, 31, 1923.
- Wakeley, C. P. G.: *Brit. M. J.*, 2, 679, 1940.

MINIMAL CRITERIA REQUIRED TO PROVE CAUSATION OF TRAUMATIC OR OCCUPATIONAL NEOPLASMS

SHIELDS WARREN, M.D.

BOSTON, MASS.

FROM THE LABORATORIES OF PATHOLOGY OF THE HARVARD CANCER COMMISSION AND NEW ENGLAND DEACONES
HOSPITAL, AND THE DEPARTMENT OF PATHOLOGY OF HARVARD MEDICAL SCHOOL, BOSTON, MASS.

THE TERM TUMOR as generally used indicates a new growth of cells which is independent of the normal restraint exerted by the body on its tissues, but may also be used very broadly to indicate any swelling regardless of its nature. However, in the medical sense, usually a new growth or neoplasm is meant. In general, tumors are classified according to the type of cell which they tend to reproduce.

The diagnosis of a tumor should not be accepted without incontrovertible proof of its nature, obtained either by pathologic examination of the entire specimen when removed, or by biopsy. So many possibilities for error exist in the diagnosis of a tumor by clinical means, even when supported by radiologic evidence, that pathologic proof should be insisted upon in addition. Not only is accurate diagnosis and classification of a tumor impossible without microscopic examination of a section obtained from the substance of the tumor, but also microscopic examination gives important information as to probable rate of growth.

Since the causation of tumors is not yet clearly understood, it is inevitable that a great mass of speculation should have been built up on this subject. In general, it can be said that there is no one cause for cancer, any more than there is one cause for inflammatory diseases, but rather there are a number of causes, some known, some unknown, which produce different types of tumor. Some tumors are clearly congenital, others are related to endocrine disturbances; still others are due to the action of specific chemical or physical agents on the body tissues; still others are of unknown origin. We have learned from observation of cases in human beings and from experiments in animals that the response to a given agent acting in a given degree is not necessarily uniform, that there are individual variations, that even in the case of highly purified hydrocarbons which have been shown to produce cancer in experimental animals, a dose that will produce a cancer in one animal may not produce it in another.¹

While trauma, in the broad sense, is any damage to the body, as ordinarily meant medically it implies the application of mechanical force to the body with sufficient violence to produce a break in the continuity of one or more of the body tissues. Repeated minor traumas may be spoken of as chronic irritation. As ordinarily used, the term traumatic cancer implies a malignant tumor which has arisen following a single mechanical injury. While there is much legal and scientific evidence that certain types of substances acting

upon the body over a period of time may produce certain types of benign or malignant tumor, so far as a single mechanical injury producing trauma is concerned, the evidence rests chiefly on reasoning from "*post hoc ergo propter hoc*"—all too often fallacious.

SECTION I—TUMORS DUE TO MECHANICAL TRAUMA

The minimal criteria necessary are: First, the integrity of the tumor site prior to injury must be established; second, the injury must be sufficiently severe to disrupt the continuity of the tissue at the site, and so initiate reparative proliferation of cells; third, the tumor must follow the injury by a reasonable length of time; and fourth, the tumor must be of a type which might reasonably develop as a result of the regeneration and repair of those tissues which had received the injury.

These criteria have been evolved gradually,^{2, 3, 4, 5} and appear sound in the light of our present knowledge.

The mere coincidence of two rare events, such as an injury in an unusual part and the subsequent development of a tumor in that part does not necessarily establish a causal relationship.

One requisite, sometimes mentioned in the literature, for the implication of a single trauma as a causative factor in tumor production is the presence of so-called bridging symptoms; that is, symptoms that continue to give evidence of the continuance of disability from the time the injury is sustained to the time the tumor makes its appearance. Among these are continuity of pain, persistence of swelling, persistence of induration or of ulceration. However, this group of symptoms is of little practical importance in establishing causal relationship with the trauma and has no bearing either from the negative or positive standpoint. Even in instances where a tumor is incited by the subcutaneous injection of carcinogenic substances in experimental animals, such as methylcholanthrene, there may be no continuity of signs from the time of injection to the time of the appearance of the induced sarcoma. On the other hand, merely because inflammation, ulceration or swelling have been present in a region, there is no certainty that the subsequently diagnosed tumor is in any way due to the conditions associated with the persisting signs and symptoms. Indeed, such signs and symptoms may actually be due to a tumor already present before the injury and masked for a time by the inflammatory and reparative processes following the trauma.

The previous integrity of the part may be assumed if its appearance and function have been normal. Only rarely is a thorough medical or radiologic examination available for reference in this regard. In many instances local trauma only calls attention to a tumor already present but unnoticed.

The adequacy of trauma is usually not difficult to determine. The injured person usually has had a careful medical examination soon after the event and there is often observation of the injured part at frequent intervals for an extended period of time. These observations may be made by the simple means of inspection and palpation or they may be supplemented by various

TRAUMA AND NEOPLASMS

types of radiologic and laboratory examinations. It may be fairly stated that trauma which fails to produce either an extravasation of blood into the tissues or a break in continuity of some of the tissues in the part affected is inadequate to be considered capable of initiating a tumor.

The time interval that may intervene between a trauma and the development of the tumor at the site is very difficult to determine. Any evidence



FIG. 1.—Multiple keratoses and epidermoid cancer due to prolonged occupational exposure to the roentgen ray.

bearing on the rate of growth of the tumor, either from clinical observation or pathologic study, is most helpful. In general, four weeks may be regarded as the minimal time for the appearance of a rapidly growing tumor following the receipt of an adequate injury. A maximal limit is difficult to set, but probably should not be over three years after the injury.

The type of tumor developing at the site of injury is important. Obviously, any dermoid or teratoid tumor, other than in the testicle, would be

automatically ruled out. Any tumor of cell type foreign to the part would be considered metastatic rather than primary.

Curiously enough, although sarcomas of bone are among the tumors most often considered as of traumatic origin, they practically never appear after the thousands of fractures that annually provide adequate trauma for tumor development.

Knox⁵ stated, in 1929: "Much of what has been published (in regard to traumatic cancer) is utterly unprofitable to read"—unfortunately, this holds as well today.

Shear⁶ notes that the application of mechanical trauma to the point of injection of methylcholanthrene exerts no accelerating effect on tumor formation and, possibly, inhibits the development of the tumor somewhat.

Much consideration has been given to tumors developing in scar tissue, thus indirectly relating the genesis of tumors to a previous trauma. Traumatic epithelial cysts are known to occur as a result of trauma driving epithelium down into the deeper tissues, but have little clinical significance.⁷ It has been clearly established that the epithelium overlying the scars of burns is peculiarly likely to become malignant. If there is a chronic persisting ulcer in the area of the scar, this is even more likely to bring about development of malignancy. Ullman⁸ states that as high as 80 per cent of these cancers developing in scars occur in the scars of burns.

Fischer-Wasels⁹ felt that only those scars following freezing or burning might be a source of carcinomatous change. This concept is too narrow, however.

The latent period before scars become cancerous may be extremely long, instances of 50 years or more having been reported.

Certain types of cancer may develop following chronic irritation,¹⁰ where repeated trauma activates degenerative and attempted reparative changes over a long period of time. While the great majority of chronic ulcers never become malignant, in a few, the attempted reparative processes may ultimately lead to neoplastic proliferation. In instances where this type of origin of tumor is alleged, the contributory negligence of the employee in permitting the chronic irritation to continue without adequate medical treatment should be carefully weighed.

One of the most difficult points to decide is whether or not trauma can change a benign tumor into a malignant one or can increase the malignancy of a cancer already present. It is, of course, obvious that if the malignant tumor is of a different cell type from the preexisting benign tumor, there can be no relationship. On the other hand, if it is a malignant variant of the same cell type the question remains open. Here, no general rule can be laid down, but in coming to a decision, it must be remembered that benign tumors may take on malignant characteristics entirely without the intervention of trauma.

I have never seen an instance in which there has been satisfactory

evidence of a single mechanical trauma converting a benign tumor into a malignant one. Many times, however, evidence appears sound that benign pigmented nevi may be converted into malignant melanomas by single or repeated injuries of various sorts. To prove aggravation of a preexisting



FIG. 2.—Multiple keratoses and epidermoid cancer developing in a coal-tar worker following some 30 years' exposure.

tumor by injury, it is, of course, necessary to establish that the tumor existed prior to the injury, that perceptible damage was done to it by the injury, and that the tumor's subsequent course was accelerated over that which would be ordinarily expected.¹¹ These factors can be evaluated only by detailed clinical and pathologic study of each case. Some evidence exists that mechanical trauma to a malignant tumor will facilitate its in-

vasion of adjacent structures and the escape of cells to establish metastases elsewhere.

To summarize, a single trauma rarely, if ever, causes a cancer, in spite of many case histories purporting to establish that fact. Repeated trauma may, rarely, produce a cancer, as may trauma to a scar. Trauma may aggravate a preexisting tumor.

SECTION II—OCCUPATIONAL TUMORS

Occupational tumors are those neoplasms that arise as a result of contact with some exogenous agent, physical or chemical, brought about by some phase of the regular work of the individual concerned, that leads to an independent proliferation of cells.

The soundest criterion for the occupational character of a neoplasm is the proof of the occurrence of a tumor of a particular type, and in a particular portion of the body, among the workers of a given industry significantly more frequently than in the general population of comparable age and sex.

As secondary proof of the occupational character of a tumor, the production of tumors in experimental animals by the suspected agent, is of great value, but it is not a prime requisite. It must be remembered that the susceptibility to various carcinogenic agents of different animal species, and even of individuals within the same species, is not at all uniform, and it is quite possible that a concentration of a given substance which is carcinogenic for man may be incapable of producing a tumor in the experimental animal. However, at times the statistical evidence that can be obtained relative to the incidence of a certain type of tumor in a certain occupation may be inconclusive and here the experimental reproduction of the tumor is of great value. In addition, of course, successful production of the tumors in animals greatly facilitates the development of preventive measures.

So far, much of the information as to the incidence of cancer in the general population is derived from mortality statistics which not only leave something to be desired from the standpoint of accuracy of diagnosis on the one hand, but give rather indefinite information as to the morbidity of the disease on the other hand. From the occupational standpoint, one is concerned primarily with cancer morbidity rather than with cancer mortality. It is to be hoped that with the passage of time an adequate mass of data as to the number of cancer cases in the general population may become available.

Sometimes it is not enough to know that an individual works in a certain general field. Thus, an oil worker may come in contact with Scotch shale oil, which has a marked tendency to produce occupational skin cancer;¹ with paraffin base petroleum oils, which are rarely associated with cutaneous malignancy;^{2, 3, 4} or with asphaltic American crude oils, which have almost never produced a skin cancer. It is, therefore, important to know the exact nature of the occupational exposure.

Occupational tumors must be sharply distinguished from tumors which

TRAUMA AND NEOPLASMS

arise spontaneously in employed individuals and have no relationship to their work. At times, the decision of the court as to whether a tumor is related to occupation is determined by the vigor and keenness of presentation of the picture in favor of plaintiff or defendant, rather than on a scientific analysis of the actual facts at issue. Unfortunately, at the present time the compensation laws in different states and also in different countries, relating to occupational tumors, vary a good deal, and, hence, are inequitable and often inadequate.

One factor which renders it particularly difficult to determine whether or not a given tumor is related to occupation is that often a long time interval may elapse between the onset of symptoms of the tumor and the exposure that occurs. This latent period may be only a matter of a few months or it may be many years. The existence of this latent period has not been adequately recognized in the framing of many of the industrial compensation laws, some of which contain time clauses, often of one or two years only. Legislation of this type is obviously unfair, as individuals being exposed to radioactive materials or betanaphthylamine at the present time may not show evidence of significant change for several years.

Another complicating aspect of the problem is that during the latent period the worker may change his occupation, and the individual who develops leukemia following exposure to benzol, or osteogenic sarcoma following the inhalation of radioactive material, may have changed occupation before the symptoms of the disease have become apparent, and may be employed in other occupations, such as building or office work, when the signs and symptoms of the disease become apparent.

Still another problem in some of the compensation laws is that specific chemicals are mentioned by name as recognized sources of occupational tumors, whereas closely allied chemical substances which may also give rise to these tumors are not named. It is wise to avoid overly specific cataloging of possible carcinogenic chemicals when framing or revising compensation laws.

The tumors formed as a result of agents encountered in the course of occupation affect a wide variety of tissues and, unfortunately, the majority of these tumors are malignant. A useful classification of occupational tumors is that given by Hueper,⁵ a modification of which is presented herewith:

I. Direct Contact Tumors:

- a. Cutaneous neoplasms caused by direct local action of mineral oil, crude paraffin, creosote, anthracene, solar rays, ultraviolet rays, roentgen rays, rays from radioactive substances upon the cellular components of the skin.
- b. Pulmonary tumors resulting from the inhalation of radioactive material, chromates, asbestos, nickel carbonyl, tarry substances.
- c. Tumors of the nasal passages and sinuses following upon the exposure to radioactive substances, chromates, nickel carbonyl.

- d. Neoplasms resulting from impingement of roentgen or other radiation on the deeper tissues.
2. Excretory Contact Tumors:
 - a. Tumors of the urinary tract resulting from an exposure to certain aromatic amines excreted in the urine.
3. Depository Contact Tumors:
 - a. Cancers of the skin associated with the deposition of arsenicals in the cells of this organ.
 - b. Sarcomas of bone, leukemia, and leukemoid reactions following the storage of radioactive material in the bones.
4. Tumors in Tissues as a Result of Parasitic Infestation:
 - a. Cancer of the bladder following bilharziasis.

The first clearly established occupational tumor is the chimney sweeps' cancer that was reported by Percival Pott,⁶ in 1775. Here we have an example of a skin cancer developing in an unusual site (the scrotum) with surprising frequency in men following a particular occupation in a particular region (the British Isles).⁷ It is interesting in this connection that chimney sweeps on the continent of Europe have not shown a high incidence of scrotal cancer similar to the English workers. This difference is due to the presence of a specific inciting factor in the type of coal that was burned in England as distinguished from that burned in Belgium or Germany, for example.

From these observations of Pott, interest in coal-tar as a possible inciting agent of tumor continued for many years. This reached its culmination in the isolation from coal-tar of a specific group of chemical products known as the carcinogenic hydrocarbons. While, as yet, their carcinogenic activity for man has not been proved, they are highly carcinogenic in certain of the animals.

The first experimental cancer produced by chemical means was the skin cancer of the ear of the rabbit produced by Yamagiwa and Itchikawa,⁸ in 1915. Thus, the experimental proof lagged more than one hundred years behind the statistical proof of the occupational character of chimney sweeps' cancer. In many other fields, however, chiefly because of the greater interest in the experimental method and the facilities for experimental work available during recent years, the time between statistical establishment of the occupational character of the disease and experimental evidence of its relation to any specific substance has been considerably lessened. Thus, Martland¹³ established, within a short time, the occupational character of the osteogenic sarcoma developing in radium dial painters.

The skin is by far the most frequent site of occupational neoplasms. This is to be expected in view of the very wide range of agents to which the skin is exposed, as contrasted with other of the tissues of the body. An important factor in the development of certain skin cancers is the amount of pigmentation that the skin contains. In general, the most heavily pigmented

skins are those which are least susceptible to damage from sunlight or other forms of radiant energy.

The mule spinner's cancer also deserves special mention. This is, again, one of the long recognized occupational tumors, and develops as a result of long exposure to oil, usually that derived from shale. Henry⁷ gives the longest period of exposure prior to onset of this skin cancer as 63 years, and the shortest 16 years.

In practically all of the occupational cancers of the skin there is a precancerous phase during which the surface epithelium is heavily keratinized and has a rather marked tendency toward the development of warts or papillomata. Frequently the openings of the hair follicles and sebaceous glands may become obstructed and active proliferation may occur in the deeper epithelial cells. There is frequently a lymphocytic infiltration of the underlying corium and the line of demarcation between the corium and the overlying epithelium becomes indistinct. Sometimes the cancers arise from foci of small, atypical epithelial cells within an otherwise not remarkable skin.

Several other types of occupational cancer deserve special mention. The cancers of the bladder developing in those working with aniline and certain of its derivatives became established as an occupational disease,⁹ in 1883. These cancers of the bladder develop as a result of the excretion of the inspired material through the kidneys and the prolonged persistence of the injurious agents in the urine held in contact with the bladder wall. Tumors of the bladder (both benign papillomas and cancers) are not only much more frequent in workers exposed to this group of compounds but develop in them at a younger age than in the general population. Thus Hueper⁵ states that over half of the number of cases of aniline tumors of the bladder develop before the age of 50, much earlier than in those not exposed to aniline and its products. The bladder tumors may develop after a relatively short exposure to the injurious agents.⁵ Thus, out of 79 malignant tumors of the bladder that developed in a group of workers, eight appeared during the first five years, and 21 during the first ten years of exposure.

Careful clinical observation and experimental work have established that many of the aniline compounds are harmless, whereas a few, as betanaphthylamine, have marked potency in producing bladder cancer.

One of the best publicized occupational tumors is the radiation cancer of the skin, from which so many of the pioneer workers with radium and roentgen ray died.^{10, 11} Fortunately, we now know enough about the character of the disease to afford protection. Repeated minor exposures to the short wave radiant energy gradually bring about pathologic changes in the skin which lead to ulcerations and keratoses; later these nonmalignant lesions take on definitely malignant characteristics. The occupational character of radiation cancer of the skin was recognized early, the first occupational cancer due to radiation being reported within seven years after the first clinical use of the roentgen ray.¹²

Certain tumors may arise in greater frequency among certain occupational groups, but are not properly considered occupational because not peculiar to that particular group of workers. Thus, the farmers in the South apparently have a higher incidence rate of skin cancer than is to be expected for a corresponding age and sex group of the entire population. However, since exposure to sunshine and weather is a factor common to all, varying only in degree, it is hardly proper to consider these skin cancers as truly of occupational origin.

Another disease, perhaps not properly occupational, is bilharziasis of the human bladder. It has been known for thousands of years that the schistosomes are peculiarly apt to involve agricultural workers when exposed to infected mud and water, in those regions where the parasitic infestation is prevalent. Conditions of the Nile delta are apparently ideal for the development of this infestation, and it may properly be considered as an occupational disease of farm workers in such localities. Larvae penetrate the skin from infected mud or water or penetrate the mucous membrane of the gastro-intestinal tract after the drinking of infected water. The larval worms reach the liver and come to adult development there. They then migrate to the venous plexuses of the pelvis, especially those of the bladder wall. Some of the eggs penetrate the mucous membrane and lie within the bladder or the rectum. Their presence leads to a chronic inflammatory reaction in the bladder wall, not infrequently with patches of leukoplakia. From this injured epithelium papillomas and cancers may arise.

In general, the mesenchymal tissues are relatively well protected against the access of the various chemical factors. As a result, none of the numerous chemical substances which may induce epithelial tumors in human beings produce either sarcomas or benign tumors of mesenchymal origin. However, it must be remembered that this apparent immunity probably rests not so much on the characteristics of the connective tissue cells themselves as on their protection from prolonged exposure.

Since Diesel engines have come into more common use, the forcing of oil deep into connective tissue and muscles by the high pressure spray is not unusual, and it will be intensely interesting to see whether, with the passing of years, some of these lesions develop neoplastic tendencies.

Undoubtedly, if we can judge fairly from our past experience, there are at present in use in industry compounds which will prove in later years to have been carcinogenic. It is of the utmost importance that every precaution be taken to protect workers from appreciable contact with substances other than those proved to be innocuous. Those workers in particularly hazardous fields, such as radium dial painters,¹³ should be carefully followed by all means of protection possible, and, in addition, frequent checks should be made of the actual conditions existing in the plant, both as to the hazards which exist under normal circumstances and those which may exist through some fortuitous chain of events.

REFERENCES

CITED IN SECTION I—TUMORS DUE TO MECHANICAL TRAUMA

- ¹ Hartwell, J. L.: Survey of Compounds which have been Tested for Carcinogenic Activity. U. S. Public Health Service. Washington, D. C., 1941.
- ² Thiem: Handbuch der Unfallkrankungen, ed. 2, Stuttgart, 1909. p. 589.
- ³ Graef, W.: Centralbl. f. d. Grenzgeb. d. Med. u. Chir., 17, 603, 1913.
- ⁴ Ewing, J.: Am. J. Surg., 40, 30, 1926.
- ⁵ Knox, L. C.: Arch. Path., 7, 274, 1929.
- ⁶ Shear, M. J.: Am. J. Cancer, 33, 499, 1938.
- ⁷ Warvi, W., and Gates, O.: Am. J. Path., in press.
- ⁸ Ullman, K., Oppenheim, M., and Rille, J. H.: Die Schädigungen der Haut durch Beruf und gewerbliche Arbeit. 3, 212, Leopold Voss, Leipzig, 1926.
- ⁹ Fischer-Wasels: Frankfurt. Ztschr. f. Path., 12, 422, 1913.
- ¹⁰ Hueper, W. C.: Occupational Tumors and Allied Diseases, Charles C. Thomas, Springfield, Ill., 1942.
- ¹¹ Behan, R. F.: Relation of Trauma to New Growths. Williams and Wilkins Co., Baltimore, Md., 1939.

REFERENCES

CITED IN SECTION II—OCCUPATIONAL TUMORS

- ¹ Leitch, A.: Brit. Med. J., 2, 941, 1924.
- ² Twort, C. C., and Twort, J. M.: Am. J. Cancer, 17, 293, 1933.
- ³ Wood, F. C.: J. A. M. A., 94, 1641, 1930.
- ⁴ Heller, I.: J. Indus. Hyg., 12, 169, 1930.
- ⁵ Hueper, W. C.: Occupational Tumors and Allied Diseases. C. C. Thomas Co., Springfield, Ill., 1942.
- ⁶ Pott, P.: Chirurgical Observations, *etc.*, Hower, Clarke and Pollins, London, 1775, p. 63.
- ⁷ Henry, S. A.: Am. J. Cancer, 31, 28, 1937.
- ⁸ Yamagiwa, J., and Itchikawa, K.: Mitt. d. med. Fakult. d. k. Univ. zu Tokyo. 15, 295, 1916.
- ⁹ Grandhomme, W.: Cited by Hueper.⁵
- ¹⁰ Haagensen, C. D.: Am. J. Cancer, 15, 641, 1931.
- ¹¹ Saunders, T. S., and Montgomery, H.: J. A. M. A., 110, 23, 1938.
- ¹² Friebe: Fortschr. a. d. Geb. d. Röntgenstrahlen, 6, 106, 1902.
- ¹³ Martland, H. S., and Humphries, R. E.: Arch. Path., 7, 406, 1929.

MINIMAL CRITERIA REQUIRED TO PROVE PRIMA FACIE CASE OF TRAUMATIC ABORTION OR MISCARRIAGE*

AN ANALYSIS OF 1000 SPONTANEOUS ABORTIONS

ARTHUR TREMAIN HERTIG, M.D.,

WITH THE COLLABORATION OF

WALTER HERMAN SHELDON, M.D.

BOSTON, MASS.

FROM THE BOSTON LYING-IN HOSPITAL, AND THE DEPARTMENTS OF OBSTETRICS AND
PATHOLOGY, HARVARD MEDICAL SCHOOL, BOSTON, MASS.

FOR YEARS the problem of traumatic abortion and miscarriage has interested obstetricians, baffled lawyers and vexed insurance companies. These three groups are brought together in the courtroom to see that justice is served in those cases involving trauma, either physical or psychic, which is alleged to have caused the premature expulsion of a nonviable fetus. It is the consensus of opinion, of at least the average conscientious expert medical witness involved, that, all too often, justice is not served and that the plaintiff is awarded damages for an abortion or miscarriage in which the trauma was, at most, only coincidentally concerned. It is the purpose of the present communication to examine and put forth the factual relationship between trauma and abortion or miscarriage.

Medically speaking, abortion is defined as the premature expulsion of a nonviable fetus. Broadly speaking, however, the definition should substitute the word "ovum" for "fetus," since, as will be shown later, almost one-half of the abortuses in the author's series contained no fetus at all; the products of conception consisting either of an empty ovisac or one occasionally containing an unformed embryonic rudiment.

To the average layman, an abortion means the termination of a pregnancy by artificial means, either criminally or self-induced. A miscarriage or "miss" on the other hand, connotes a spontaneous termination of a previable pregnancy. To complicate the terminology still further, the average medical person regards an abortion as covering the period up to the sixteenth week of gestation and a miscarriage as covering the period from the sixteenth to the twenty-eighth week of gestation, the average period at which the fetus becomes, theoretically, viable. It is clear, therefore, that the term abortion, when used in the broadest medical sense, includes all previally delivered ova although in a more restricted sense refers to only the first 15 weeks of gestation. *These factors of terminologic confusion* must be kept in mind by all three of our interested groups when conferring, either with one another or with the lay public. Hereinafter the term abortion will be used in the broadest medical sense.

That there is a real relationship between trauma and abortion is ad-

* Aided by a grant from the Carnegie Corporation of New York, and the Theodore E. Brown Research Fund of the Boston Lying-in Hospital.

mitted by all qualified medical experts in the field (Taussig¹). However, the number of *bona fide*, traumatically caused abortions is much rarer than is generally supposed by the average lay, legal and medical public. It is proposed to cite the evidence for this relationship by analyzing a series of abortuses examined in the Pathological Laboratory of the Boston Lying-in Hospital, either by or under the immediate supervision of the author.

MATERIAL AND METHODS

The period encompassed in the study is from February, 1936, to December, 1941. During this six-year period a total of 1416 consecutive abortuses were carefully examined from an embryologic as well as a pathologic point of view. Many of these 1416 cases have been submitted by physicians in Boston, although moderate numbers of specimens have been received from hospitals and physicians in other communities. Since a good many of the physicians on the staff of the Boston Lying-in Hospital submit every spontaneously aborted ovum from their private practices, it is felt that this material, with the specific exceptions of hydatidiform moles and criminal abortions, is representative of the variety of pathologic conditions associated with spontaneous abortion in general.

Of these 1416 abortuses, 1000 were selected as the basis of the present report. The criteria of selection are based merely on the completeness of both the clinical history and the pathologic material submitted. Obviously, an incomplete abortion, containing only a tiny bit of curetted decidua and a few chorionic villi is not sufficient material upon which to base valid conclusions for a study of this sort. Furthermore, a series of 63 hydatidiform moles examined in the laboratory during this period are excluded from the present study since they would seriously invalidate the statistical value of these data. Such moles are rare (approximately 1:2000 cases of pregnancy) but are prominent in the total series because the author is especially interested in that subject and has collected them from all over the country. The 1000 selected cases, therefore, represent a consecutive series of abortuses which are complete enough, both as to history and material, so that valid conclusions may be drawn from their study. The round number chosen also facilitates figuring percentage values. The general technic used in the examination of this material is detailed in Mall and Meyer's² classic work reporting the pathologic ova in the first 1000 accessions to the world-famous embryologic collection of the Carnegie Institution of Washington.* In 1940, the author³ published certain data from the first 1027 abortuses examined at the Boston Lying-in Hospital pertaining to the genesis of hydatidiform mole. Detailed notes on the technic of examining these abortuses are given in that paper.

* It was the privilege of the author to spend a year in the Department of Embryology of that Institution under the guidance of Dr. Franklin P. Mall's successor, Dr. George L. Streeter, to whom the author is greatly indebted for instruction in the methods of studying normal and abnormal human ova. For the past nine years, since the initial year of study there, the author has collaborated in the work of that laboratory, now under the direction of Dr. George W. Corner.

Since it is the consensus of medical opinion that at least ten per cent of all pregnancies terminate in spontaneous abortion, and that only rarely are such abortions caused by trauma, the main emphasis in this paper will be to point out the apparent primary etiology in 1000 abortions and to discuss in detail the relationships of trauma to abortion in the 13 cases of this series in which trauma of any sort antedated the abortion. It should be noted here that in only one of these 13 cases was external trauma, an automobile accident, responsible for the abortion. In view of the frequency of spontaneous abortion and the rarity of true traumatic abortions, it becomes of the greatest importance to evaluate mere coincidental trauma in spontaneous abortion. The thesis of this report, therefore, may be summed up by stating that, in the opinion of the author, the plaintiff in a case of alleged traumatic abortion must present proof of the presence of a normal pregnancy at the time of the trauma and that the abortus shows objective clinical, embryologic and pathologic evidence of the relationship to the trauma.

MAIN CLASSIFICATION OF MATERIAL

The classification followed in studying these abortuses is essentially the same as that devised by Mall (Mall and Meyer²). Pathologic ova in Mall's original classification are those in which the embryos are absent, very defective or macerated. The author has modified this classification by excluding the macerated embryos from the pathologic group since, broadly speaking, these embryos are anatomically normal but have died in utero for one reason or another. Hence, in this series many so-called normal ova contain macerated embryos although the ovisacs show various pathologic changes which account for the death of the embryo and subsequent abortion of the ovum.

The following figures are a crude breakdown of the 1000 cases with respect to the main embryologic and pathologic features shown in each specimen, although each subgroup will be subsequently discussed more in detail:

I, OVULAR FACTORS:

1. Pathologic ova, with absent or defective embryos.....	489
2. Embryos with localized anomalies.....	32
3. Placental abnormalities.....	96

II. MATERNAL FACTORS:

1. Criminal abortions.....	21	
2. Uterine abnormalities.....	64	
3. Febrile and inflammatory diseases.....	20	
4. Miscellaneous.....	12	
5. Anatomically normal ova (classified).....	265	
6. Trauma (automobile accident).....	1	383
		<hr/>
		1000

I. OVULAR FACTORS

1. Pathologic Ova

These specimens constitute the largest single group in the series (48.9 per cent) and are the typical "blighted ovum" of the clinician. They are classified in more detail as follows:

Group I.—*Villi Only*: This material contains only chorionic villi, whether normal or abnormal. Obviously, this group is one of convenience only, since it merely classifies the material submitted, which may or may not adequately represent the relationship between maternal and ovular tissues. This group, therefore, includes curettings from cases of incomplete abortions. Actually very few of the large number of such cases in the total series of 1416 abortions are included in this study because of the obvious incomplete nature of the material.

Group II.—*Empty Chorionic Vesicle*: This type of specimen when intact (as it often is) represents the most pathologic type of ovum with which the pathologist has to deal. There is no derivative of the inner cell mass; that is, of the portion of the fertilized ovum destined to form the embryo. If the chorion is ruptured, one might have reasonable doubt about the essential pathologic nature of the ovum; that is, the normal embryo with its surrounding amnion may have been lost during the abortion. However, if trauma has produced such an artefact in an otherwise normal ovum, one can usually see evidence of the torn stump of a normal umbilical cord with its radiating vessels.

Group III.—*Chorion Containing Empty Amnion*: This type of ovum is only slightly less pathologic than the previous one, there being no evidence of an embryo, although the amnion is present. Members of this group are, likewise, valid if intact—as they often are—although if ruptured, erstwhile normal ova with the embryos missing can usually be detected and differentiated from true Group III specimens.

Group IV.—*Chorion and Amnion Containing Nodular Embryo*: This type is truly pathologic, as the embryonic mass consists merely of a disorganized group of embryonic cells. Artefacts in this group would consist of the macerated remains of an otherwise normal umbilical cord within either a ruptured or intact amnion.

Group V.—*Chorion and Amnion Containing Cylindric Embryo*: If the head end of the embryo can be recognized, even though it does not possess any other features of an embryo, such a specimen is valid for this group. (It is quite rare in the author's experience.)

Group VI.—*Chorion and Amnion Containing Stunted Embryo*: It is possible to recognize the embryonic form, although it is much smaller than it should be for the menstrual age of the specimen. In addition, one or more portions of the embryo are atrophic, deformed or degenerated. These embryos are usually not macerated. This is a valid group whether the chorion and amnion are ruptured or not, since the embryo has to be recognized before the specimen may be placed in this category.

The vast majority of this large and important group, destined for abortion, whether there is associated external trauma or not, belongs in Groups II, III and IV. They tend to abort during the tenth week of gestation. Evidence recently accumulated by the author,⁴ in collaboration with Dr. John Rock, show that these pathologic ova are deficient from the early stages of development before the patient has any knowledge that she is pregnant.

2. Embryos with Localized Anomalies

These specimens constituted 3.2 per cent of the total series. The congenital anomalies include many of the common deformities of the nervous system such as spina bifida, meningo-encephalocele, anencephaly, etc., which may go to term but are incompatible with continued extra-uterine existence. Other anomalies are also found in the group such as deformed extremities. That these particular anomalies are responsible for the death of the embryo and subsequent abortion of the ovum is not rigidly maintained. It is significant, however, that the incidence of congenital anomalies is 4.7 times greater in this series than in Murphy's⁵ series of stillborn and living fetuses which went to term. Hence, the presence of a congenital anomaly in an aborted fetus must be *prima facie* evidence of some general ovular abnormality which is expressed by the presence of the localized anomaly seen in the specimen.

3. Placental Abnormalities

This relatively large group constitutes 9.6 per cent of the total. Its inclusion in the main group of abortions due to ovular factors may be questioned since the etiology of the single largest group, the circumvallate placenta, is not entirely clear. However, since the circumvallate placenta, which tends to separate prematurely and, hence, causes abortion and premature labor, is an abnormal placenta, whatever its cause, it is included here under the general heading of abortions due to ovular factors.

The general group of placental abnormalities, together with the number of cases of each variety are listed as follows:

a. Circumvallate placenta	45
b. Hypoplasia of the placenta	20
c. Placenta membranacea, partial	2
d. Velamentous insertion of umbilical cord	1
e. Hypoplasia of amnion	1
f. Rupture of marginal sinus	3
g. Premature senility of placenta	4
h. Bcrus' mole (intraplacental hematomata)	19
i. Succenturiate lobe with total infarction	1
Total	96

The common denominator with respect to the cause of the abortion in most of this group is death of the fetus and subsequent expulsion of the ovum. Some of the circumvallate placentae, when they separate prematurely at their margin, are associated with premature labor, in which case the embryo is still living when delivered.

II. MATERNAL FACTORS

1. Criminal Abortions

This group is necessarily small and constitutes 2.1 per cent of the total. It is expected that criminally induced abortions would not be numerous in a group of spontaneous abortions submitted to the pathologist in an attempt to discover the cause of the abortion. However, the author has been interested in the pathologic sequence of events in criminally induced abortions and has attempted to acquire material, thus accounting for the few cases of this type among the group of otherwise spontaneous abortions. The figure of incidence, therefore, is entirely erroneous and much lower than actually exists throughout the country. Suffice it to say that the pathologic picture is often one of artificial premature rupture of the membranes followed by acute bacterial inflammation of the chorion, amnion, placental villi and decidua.

2. Uterine Abnormalities

This is a distinct group constituting 6.4 per cent of the total. The various subdivisions of this group, together with the number of cases of each are as follows:

a. Low implantation of placenta	56
b. Placenta accreta	2
c. Bicornuate uterus	2
d. Multiple leiomyomata of uterus	1
e. Retroversion of uterus, fixed	3
Total	64

It may be questioned as to why the low-implanted placentae (including five definite cases of placenta previa) should be considered as due to any maternal factor. The reason for assuming this, as yet unproved, relationship is because of the high incidence of placenta previa in multiparae. It seems unlikely that the fertilized ovum of a multigravida is any different from that of a primigravida although the postpartum uterus of the former never quite involutes back to its nulliparous state.

3. *Febrile and Inflammatory Diseases*

This small but important group constitutes 2 per cent of the total series and includes local bacterial inflammation of the endometrium, both acute and chronic as well as febrile states from various causes. The cases are listed as follows:

a. Bacterial inflammation of decidua, acute.....	12
b. Small pox.....	1
c. Pyelitis with horseshoe kidney.....	1
d. Fever of unknown etiology.....	5
e. Chronic endometritis.....	1
	<hr/>
Total.....	20

It is worthy of comment that local inflammation plays a relatively small part in the etiology of spontaneous abortion. This is in contrast to the views advanced by Mall and Meyer,¹ who ascribed to inflammation a prominent rôle in the causation of abortion. It would appear that they misinterpreted the leukocytic response to sterile decidual necrosis following thrombosis of sinusoids—a universal finding in all spontaneous abortions of whatever etiology.

4. *Miscellaneous*

This small and heterogeneous group (1.2 per cent, is formed as a matter of convenience only. There is no relationship between any of the following group of cases:

a. Radiation effect on ovaries.....	2
b. Erythroblastosis fetalis.....	3
c. Surgical removal of corpus luteum.....	4
d. Blood dyscrasia.....	1
e. Interference with circulation of cord.....	2
	<hr/>
Total.....	12

5. *Anatomically Normal Ova (classified)*

This is the next largest group in the series and constitutes 26.5 per cent of the total. These abortuses all have one factor in common; namely, an anatomically normal ovum to which various things have happened *in utero*. The following tabulation gives the main subdivisions of this large and, in general, unsatisfactory group:

a. Anatomically normal ova without disease.....	227
Fetus, macerated.....	146
Fetus, nonmacerated.....	74
Fetus, by history only.....	7
	<hr/>
	227
b. Acute chorionitis, consistent with spontaneous premature rupture of membranes (fetus macerated in 9 and normal in 5).....	14
c. Positive Hinton and Wassermann tests.....	3
(The syphilis was probably not responsible for the abortion)	
d. Infarction of placenta, extensive.....	13
(All fetuses were macerated)	
e. Toxemia of pregnancy.....	5
(Fetus macerated in 3 and normal in 2 cases)	
f. Trauma (internal).....	1
(Two successive biopsies on sterility patient not known to be pregnant)	
Exploratory celiotomy.....	1
Intrauterine lipoidal injection, 7 weeks prior to last menstrual period.....	1
	<hr/>
Total.....	265

It is obvious that the large number of cases (227) in group "a" show no satisfactory

cause for their abortion. That the placenta prematurely separated in some of the cases (27) and that the patient then went into premature labor is only begging the issue. Of course, nearly two-thirds of this group showed macerated fetuses, a perfectly adequate cause for the abortion but the cause of the intra-uterine fetal death is still obscure.

Those cases in group "b" who prematurely rupture their membranes with subsequent infection of the ovisac and expulsion of either a dead or living fetus are, in the last analysis, unexplained. What causes the membranes to rupture prematurely is unknown, although it is the impression of the author that the ovisac is too small in many cases as compared to the size of the growing fetus.

It is interesting to note the relative paucity of cases complicated by syphilis. In older dissertations on abortion, syphilis was prominently mentioned as a cause but at the present time it would seem to play no etiologic rôle in spontaneous abortion.

Toxemia of pregnancy is uncommon during the period of gestation concerned in the cases in this study. It may kill the fetus directly, by means as yet unknown, or it may cause fetal death by toxic premature separation of the placenta.

The one case of internal uterine trauma, aside from those in the criminally induced group, is of interest from a medicolegal point of view. It illustrates that extreme care must be exercised in doing endometrial biopsies on sterility patients, especially after the period of implantation of the ovum. Since most, if not all sterility patients may theoretically be pregnant during the last half of the menstrual cycle, it is possible that a biopsy performed after the 19th to the 22nd day may mechanically interrupt a pregnancy which, as yet, necessarily, gives no evidence of its presence.

The second case in group "f," the abortion following an exploratory celiotomy, is of interest. The patient had been widowed for three years (a factor of probable importance in this case). Since the last menstrual period was not known, or admitted by the patient, and because the periods were alleged to have been regular but scanty, the enlarged uterus was thought, clinically, to have been a fibroid uterus. The patient was flowing at the time of the exploratory celiotomy, which revealed a normal pregnant uterus of approximately $3\frac{1}{2}$ to 4 months gestational age. A week following the operation the patient miscarried a normal but macerated fetus of 16 weeks gestational age. The cord was about the neck twice, although this was probably not of etiological significance in the death of the fetus since a dead fetus may move about passively in the uterus due to uterine contractions and general activity on the part of the patient. Whether the operation caused the abortion cannot be proven. There are no data by which this factor can be judged since the menstrual age of the pregnancy could not be accurately ascertained. In view of an atypical story by a widow of three years standing, who was bleeding at the time of operation, it is justifiable to wonder, at least, if this is not a traumatic abortion of the self-induced or criminal type rather than due to the operation.

The final case in group "f" is also of medicolegal significance in that the sterility patient had a lipiodol injection into the uterus and tubes seven weeks prior to the last menstrual period before she became pregnant. She aborted a normal but macerated eight weeks fetus and chorion at ten weeks and five days after the last menstrual period. It is difficult to see what relationship, if any, the lipiodol uterotubogram had on the subsequent abortion unless one postulates that the oily substance, which is known to persist for some time in the tubes, affected the fertilized ovum on its passage through the latter. However, the fertilized ovum was of such vitality that it developed to the stage of a normal eight weeks pregnancy at which time the embryo died. It seems unreasonable to assume that the theoretically unfavorable environment created by the lipiodol persisting for seven weeks in the tubes, could have had a delayed effect on the ovum. It is well recognized among teratologists that the developing ovum is affected relatively soon after its exposure to unfavorable environments. However, one cannot absolutely rule out the delayed effect of lipiodol and so the case is included in this general group.

TRAUMATIC ABORTION

6. Trauma (automobile accident)

This single case of a normal twin pregnancy which aborted following, and because of the patient's involvement in, an automobile accident is a classic example of a *bona fide* traumatic abortion. It satisfies the criteria reserved for such cases by the conscientious medical expert and is, therefore, deserving of a detailed history.

This patient was a 22-year-old gravida I, para 0, whose last menstrual period occurred on November 24, 1937, 12 weeks and two days prior to her involvement in an automobile accident. This occurred while sitting in a stationary automobile which was struck from the rear by another car. The patient was excited and emotionally upset, although there was no mention in the clinical history of definite bodily injury. Seven hours after the accident the patient began to have painful uterine cramps followed in five hours by slight vaginal bleeding. Morphine, grains $\frac{1}{2}$, given in two divided doses one hour apart, failed to alleviate the uterine pain which, after six hours, became steady and was localized in the right lower quadrant. The patient experienced a chill at this time but had no elevation of temperature. She vomited once. The pulse was 82 and the blood pressure 120/60. Physical examination, performed by an obstetrical consultant, showed a nontender pregnant uterus of approximately four months gestational age. The uterus was, therefore, somewhat larger than the menstrual history would indicate. (This was later shown to be due to an excess amount of amniotic fluid and normal twin fetuses, each of which was normal in size and development for the stated duration of pregnancy.)

The patient was admitted to the hospital 11 hours after the onset of uterine pains (labor). She soon ruptured her membranes spontaneously and delivered normal twins an hour later; 19 hours after the accident and 12 hours after the onset of labor.

Pathologic examination revealed an anatomically normal twin pregnancy whose fetuses each showed the expected degree of development for their menstrual age (12 weeks and three days). The menstrual age of aborted embryos is determined by reference to tables of embryonic development compiled by Dr. George L. Streeter,⁶ recently retired director of the Carnegie Institution of Washington's Department of Embryology.

There is no reasonable doubt but what the accident initiated labor. Whether it did so by means of direct trauma or the psychic shock incident thereunto is impossible to say. It is quite possible that the increased distention of the uterus due to the twin pregnancy, made the organ more irritable and hence more susceptible to the factor or factors which initiate labor. Be that as it may, it would appear that this is a case of *bona fide* traumatic abortion for which the patient should, with justice, be compensated. It is of interest that as the result of this accident the patient received \$700 to \$800 in addition to having her hospital bill paid.

ABORTUSES WITH A HISTORY OF ANTECEDENT TRAUMA

In the entire series of 1000 abortions concerned in this study, there are nine cases in which external trauma of some variety was recorded prior to the expulsion of the ovum. Five cases proved, on pathologic and embryologic examination, to have passed pathologic or defective ova which would undoubtedly have aborted irrespective of any trauma, while four cases showed placental defects which caused the abortion.

Four of the patients who passed pathologic ova had taken long automobile rides a week or ten days prior to the abortion. Inasmuch as patients are warned against this practice, it is of some interest to note that, at least in these four cases, the automobile ride bore no causal relationship to the

abortion; none of the ova contained any embryo (except a nodular one in one case) and, hence, all were destined to abort.

The fifth case, involving a pathologic ovum, is deserving of special comment because the patient experienced a back strain, a fall and a death within the family prior to her passage of a typical blighted or pathologic ovum. The latter consisted of the most pathologic variety encountered—the empty chorionic shell without vestige of amnion or embryo. Embryologically, this ovum had been abnormal prior to the ninth or tenth day of its development, at which time the amnion begins to form. It is obvious that none of these various forms of trauma, including the psychic shock of the death in the patient's family, had anything to do with the subsequent abortion.

The four remaining cases in which the abortuses showed placental defects can be discussed as a group. The traumata associated with these cases are as follows: a long automobile ride just before abortion, psychic shock or trauma suffered as the result of being near an automobile accident two days prior to abortion, involvement in an automobile accident six weeks prior to abortion and a severe fall at home two days prior to abortion. All pregnancies progressed normally until the 19th to 20th weeks. All patients passed normal fetuses, two of which were macerated, one was normal and one was not submitted although it was said to be normal. The placentae all showed varying degrees of circumvallate formation; a developmental defect of the placenta, probably associated with too shallow implantation of the ovum in the endometrium. This defect of implantation, with its resulting poor maternal blood supply, allows only a relatively small area of the chorion, or external shell of the ovum to form a placenta. In order for this small patch of placental tissue thus formed to supply the fetus with sufficient food and oxygen, the lateral margin of the placenta grows radially and in so doing causes premature separation of the placenta itself.

Inasmuch as implantation of the fertilized ovum occurs on the nineteenth to the twenty-second day of the menstrual cycle,^{4, 7} or about a week prior to the patient's knowledge of her pregnancy, it is obvious that trauma occurring after pregnancy has been established cannot be responsible for abnormalities of the placenta due to faulty implantation of the ovum.

DISCUSSION

From the foregoing data it is clear that antecedent external trauma or psychic shock may appear in the history of a case of abortion. That trauma is only rarely etiologically related to the abortion is also evident from an analysis of the 13 cases in which antecedent trauma is recorded; only one of these abortions was caused by external trauma. When trauma is an etiologic factor in an abortion it must immediately precede, by a matter of hours, the onset of the sequence of events that results in an expulsion of a normal ovum.

It is obvious, furthermore, that in the case of a *bona fide* traumatic abortion, the ovum must be shown to be developing normally up to the time at which

TRAUMATIC ABORTION

the trauma occurred, since there are many other factors independent of trauma which can and do cause abortion. Since true traumatic abortion is such a rarity and spontaneous abortion such a common occurrence, even though antecedent trauma may be recorded in proven spontaneous abortions, it is mandatory that the normality of the pregnancy be proven in cases of alleged traumatic abortion. In the light of the findings in this series of abortions, it becomes obvious that the normality of a given pregnancy cannot be determined by clinical examination alone. The normality of the abortus by someone expert in this special field of pathology. Finally, it would seem to the author that the burden of proof of the relationship between any given trauma and the subsequent abortion be upon the person who alleges that the particular trauma caused the resulting abortion.

To verify the relationship of trauma to abortion the author consulted seven obstetrical specialists in Boston, all of whom are members or emeritus members of the Obstetrical Society of Boston. They were questioned as to the number of *bona fide* cases of traumatic abortion encountered in their obstetrical experience. The number of cases and their years in practice are as follows:

1 case	in 38 years
3 cases	in 28 years
2 cases	in 27 years
0 cases	in 25 years
0 cases	in 22 years
0 cases	in 10 years
0 cases	in 7 years

The specialists who had taken care of such traumatic abortion cases were in unanimous agreement that the onset of signs or symptoms leading to abortion followed the causative trauma within minutes to hours. The initial sign may have been either rupture of the membranes or vaginal bleeding followed by uterine cramps and expulsion of the normal ovum. The etiologic trauma took such diverse forms as extreme exertion during a severe thunder storm (1 case), automobile accidents (3 cases), climbing the mast of a sailboat during a race in order to fix a broken halyard (1 case), and a severe paroxysm of coughing due to whooping cough (1 case).

The history of one additional case has come to the author's attention recently. The patient was thrown clear of an automobile, sustaining lacerations of the right thigh and vulva together with a fractured skull. When picked up soon after the accident she was bleeding profusely from the vagina due to an inevitable abortion which was completed in the hospital. The ovum was normal.

SUMMARY

The analysis of 1000 cases of abortion, selected as to the completeness of their clinical history and pathologic material, shows that external trauma and/or the psychic shock associated with it did, in one case, initiate the

sequence of events resulting in the abortion of a normal twin ovum. Careful pathologic and embryologic examination of 11 abortuses from patients who gave a history of antecedent trauma showed adequate natural causes for the abortions—the trauma in such cases being purely coincidental. The remaining 988 abortions showed no etiologic relationship to external trauma although 21 of them were criminally induced, and one normal ovum aborted as the result of two endometrial biopsies done on a sterility patient prior to her first missed period.

CONCLUSIONS

1. A series of 1000 abortions are reported and their etiology determined by clinical history, embryologic and pathologic examination.

2. One case of a normal twin pregnancy aborted at 12 weeks and three days as the result of external trauma and/or the resulting psychic shock resulting from an automobile accident.

3. Eleven cases of abortion preceded by various external traumata are analyzed and shown to be due to natural causes.

4. The remaining 988 abortions (including 22 induced by internal uterine trauma) were due to a variety of naturally occurring ovular and maternal factors.

5. The collective experience of a representative group of Boston obstetrical specialists is reported with respect to abortions occurring as the result of external trauma and/or psychic shock.

6. A *bona fide* traumatic abortion is one in which the abortus was anatomically normal in development up to the time at which the external trauma and/or psychic shock occurred. If this predicate cannot be proven, we must regard the evidence of traumatic causation as conjectural and speculative, and suspect that the abortion was a spontaneous one due to pathologic causes.

7. Minutes to hours is the time interval between the occurrence of the external trauma and/or psychic shock which initiates the sequence of events resulting in the expulsion of a normal ovum.

REFERENCES

- ¹ Taussig, F. J.: Abortion, Spontaneous and Induced: Medical and Social Aspects. C. V. Mosby Company, St. Louis, 1936.
- ² Mall, F. P., and Meyer, A. W.: Studies on Abortions: A Survey of Pathologic Ova in the Carnegie Embryological Collection. Contributions to Embryology (No. 56), 12, 1921.
- ³ Hertig, A. T., and Edmonds, H. W.: Genesis of Hydatidiform Mole. Archives of Pathology, 30, pp. 260-291, 1940.
- ⁴ Hertig, A. T., and Rock, J.: Some Aspects of Early Human Development. American Journal of Obstetrics and Gynecology, 44, 973-983, 1942.
- ⁵ Murphy, D. P.: Congenital Malformations. Privately printed by the Gynecologic Hospital Institute of Gynecologic Research of the University of Pennsylvania.
- ⁶ Streeter, G. L.: Weight, Sitting Height, Head Size, Foot Length and Menstrual Age of the Human Embryo. Contributions to Embryology (No. 55), 11, 1920.
- ⁷ Hertig, A. T., and Rock, J.: On the Development of the Early Human Ovum: With Special Reference to the Trophoblast of the Previlous Ovum. Read before the Chicago Gynecological Society, Chicago, Illinois, December 18, 1942.

THE RELATION OF TRAUMA TO DIABETES*

ELLIOTT P. JOSLIN, M.D.
BOSTON, MASS.

CERTAIN FUNDAMENTAL FACTS are herewith recorded, essential for a proper understanding of diabetes, and following these are various concepts which will serve as a summary of the relation of trauma to the disease.

FUNDAMENTAL FACTS CONCERNING DIABETES

1. Diabetes is an hereditary disease, characterized by an increase of sugar in the blood and the excretion of sugar in the urine; it is dependent upon the loss or decrease of the insulin secreted by the islands of Langerhans of the pancreas and is functionally interrelated with other endocrine glands, particularly the pituitary but also the adrenal, thyroid, and the liver.

2. Proof of the diagnosis of diabetes is all important. The lack of accurate, diagnostic tests in the past and the failure to distinguish between glycosuria and the disease (diabetes) renders valueless most of the older literature.

3. Diabetes is universal. It ranks eighth as a cause of death in the United States, and approximately one individual in 165 of the total population has the disease. No age, sex, race or social status is immune. Its incidence is increasing and presumably will continue to grow until the average age at death of the population exceeds the date of onset of the disease which it is most apt to begin. This makes the decade 44-55 years, in relation to the time of the trauma a crucial factor. This is especially true if influences favoring the development of diabetes already exist. The onset of diabetes is usually indefinite, but it may be sudden and in the span of 24 hours, and was so classified by me in 1.3 per cent of one series of 7000 of my cases.

4. Legal proceedings, based upon trauma, during the course of diabetes either should be avoided or entered upon after unusual deliberation by employers from hiring or even keeping in their employ other diabetics and diabetics. A diabetic may go to court and win his suit, but this discourages puts off the day when the diabetic can enter government service or secure

* The author, with his associates, has written a more detailed discussion of Trauma and Diabetes in the volume Trauma and Disease, Brahdly and Kahn, 2nd Ed., Lea & Febiger, Philadelphia, 1941, pp. 536-589; also in The Treatment of Diabetes Mellitus, Lea & Febiger, Philadelphia, 1940, 7th Ed., pp. 76-87. In each of the foregoing articles references to the literature and citations of cases are numerous, but in this article I have tried to approach the subject from a somewhat different and more confident point of view because of the 22,258 diabetic cases having consulted my associates and me and, also, because recent advances in diabetic knowledge have confirmed many earlier suppositions. In general, the literature cited here is in addition to the bibliography of 83 or more references in the most recent of the above publications.

insurance. There are about 800,000 diabetics now living in the United States and in a peculiar sense each one is his "brother's keeper."

CONCEPTS CONCERNING TRAUMA AND DIABETES

1. The thesis that trauma *de novo* can cause diabetes has steadily lost support with the expanding knowledge of the nature of the disease.

2. But evidence has accumulated to show that trauma indirectly can activate, or accelerate the appearance of a latent diabetes in the hereditarily predisposed, particularly if accompanied by infection, reduced muscular exercise, gain in weight or overeating.

3. Trauma in the course of diabetes has grown in importance, because the duration of the disease has trebled, thus lengthening the period of exposure. Moreover, the danger of exposure to trauma is intensified each successive year a diabetic lives, because time is provided for the disabling complications of the disease to appear and the physical infirmities of the normally aging process to advance.

The tissues of a diabetic are more vulnerable than those of a non-diabetic.

4. Trauma may make the diabetes more severe, but this effect is not necessarily permanent.

5. Emotional, nervous, so-called neurogenic diabetes, as von Noorden well said, was put "into the grave" by the Great War, and there it is likely to remain unless exhumed during the present conflict.

6. To prove that trauma is the cause of diabetes in any individual case evidence must be at hand to show (a) that the disease did not exist before the trauma; (b) that the trauma was severe, injuring the pancreas; (c) that the symptoms and signs of the disease developed within a reasonable period following the trauma, the etiologic importance of the trauma waning with the prolongation of the interval; and (d) that the symptoms and signs of diabetes were not transitory but permanent.

7. This question of trauma as the cause of diabetes should be kept absolutely distinct from the question of compensation of an individual who is found to have diabetes following an accident. Too often, especially in foreign publications (Lommel, Troëll) the two are confused, and for social and governmental insurance reasons the court sitting in judgment on a case may vote to give the insured the benefit of a doubt which has no factual basis. Many European countries are saturated with social accident insurance, and if a citizen is not actually in the employ of the government, at least he expects a liberal interpretation of social or insurance benefits.

THE DISEASE DIABETES

1. *Diagnosis.*—The diagnosis of diabetes depends upon the demonstration not only of glucose in the urine (glycosuria), but also of a per cent of glucose in the blood (glycemia) of 130 mg., or above, when the subject has been without food for five or more hours or of 170 mg. (hyperglycemia),

TRAUMA AND DIABETES

or more, after intake of food. Insurance companies are suspicious of 120 mg. per cent fasting, and some clinicians raise the boundary line after food to 180 mg. per cent. Fifteen (14.8) per cent of all cases consulting me during the period 1897 to 1935 for a possible diabetes proved on investigation not to be diabetic. All but 32 of these 1946 cases were traced, and the diagnosis, in the course of years, was subsequently changed to diabetes, usually mild in character, in 193, but only in approximately a third of this number was it altered if the diagnosis was originally based on glucose tolerance tests. Other sugars, levulose, lactose, and pentose are occasionally found in the urine, but they have no connection with true diabetes. Glycosuria (non-diabetic), levulosuria, lactosuria and pentosuria are harmless states. The common tests for glucose in the urine are reliable and seldom subject to error, but this does not hold true for tests of the blood sugar which are more complicated and to be diagnostic must be carried out with special precautions regarding technic and reagents. The diet and the physical status of the subject at the time of the examination are of prime importance, else the reliability of the diagnosis is open to question.

Proof of the diagnosis of diabetes is all-important. Accurately planned and well-meaning conclusions concerning trauma and diabetes in the past today fall flat because the early authors did not have the facilities to distinguish between glycosuria and diabetes. Konjetzny and Weiland's conclusions, in 1915, upon glycosuria, diabetes and fractures, although still often quoted, are invalidated by the modern studies of Timpe, supported by tests of the blood sugar.

This very month a priest, Case No. 22290, told me, in applying for a Chaplaincy, he passed the Selective Service, including an examination of the urine, but two weeks later diabetes was discovered because the test was performed soon instead of long after a meal. Case No. 2063, with diabetes of 23 years standing, onset at 14 years of age, wrote me he also passed his entire physical examination including urine test, but was finally disbarred when he revealed his diabetes. He died suddenly in December, 1942, presumably of coronary thrombosis. The insurance policy which he obtained one year before was obviously cancelled.

2. *Did Diabetes Precede the Trauma?* Whenever the question of trauma as the cause of diabetes existed before the accident. For one should establish whether diabetes existed before the accident. For this purpose a rigorous search for symptoms and signs of the disease should be made as well as for the existence of factors predisposing to its development so that the date of onset can be determined with reasonable accuracy. This is not the place to discuss the symptoms and signs of diabetes, which are to be found in text books of medicine or in the monographs of Joslin, Root, White and Marble, and of Wilder, but some of the statistical data and influences provocative of the disease deserve attention.

What are the chances of an individual in the United States already having

diabetes at the time of an accident? The National Health Survey computed the number of diabetics in this country, in 1938, as at least 660,000, but in my opinion for this year, 1943, it is nearer 800,000. Diabetes occurs at any age, but with increasing proportion as one grows older. The frequency is 1 in 2500 up to 15 years of age in either sex, and reaches 1 in 70 for males and 1 in 45 for females at 65 years and above. Among Jews from early middle life on the incidence is higher, perhaps twice as great, being highest of all among Jewish women between the ages of 55 and 64, the proportion of deaths from diabetes to total deaths among Jews in New York City, in 1933, being 11.5 per cent. The draft has stimulated the finding of new cases not alone in the young but at all ages. In 1900 diabetes was 27th as a cause of death; in 1938, it was ninth, but in 1941 it advanced to eighth place. Diabetics are living longer and longer. Tabulations made by the Statistical Department of the Metropolitan Life Insurance Company, based on my own fatal cases, show that the duration of life of the average diabetic advanced from 4.9 years between 1898-1914 to 14.3 years between 1940-1942. The expectancy of life for a diabetic, also computed for my series, is about two-thirds that of the population as a whole for comparable age-groups.

A positive heredity also increases the chances of the individual having diabetes. Pincus and White conclude from their studies that at least 25 per cent of the population carry the hereditary gene for diabetes and are, therefore, predisposed to the disease. Heredity is greatest in identical twins, reaching 70 per cent; in cases with onset in childhood and living 20 or more years it is 62 per cent, and for 1800 diabetics on my service at the George F. Baker Clinic at the New England Deaconess Hospital in 1941 was 40 per cent.

A diabetic heredity makes an individual susceptible to the disease, but of all factors predisposing to its development by far the most potent is obesity. It precedes the onset of diabetes in more than three-fourths of the cases, and from 40 years onward reaches a still higher per cent. Among 2000 of my own cases of diabetes, not one occurred who was more than 30 per cent underweight, and in Adams' series of 1000 cases at the Mayo Clinic, no patient developed the disease who was more than 20 per cent underweight.

The type of onset of diabetes is of great significance no matter whether it is indefinite in 85 per cent of the cases, or sudden, within the space of 24 hours, in a trifle over one per cent, as already mentioned. Whereas the slow, unobtrusive onset presents many a puzzling problem before an approximately correct date can be fixed, the cases of sudden onset offer the best evidence for a *post hoc propter hoc* argument. Eight thousand (one per cent of 800,000) or more cases with a sudden start of their disease are now available in the United States. What opportunities they afford for traumatic, diabetic exploitation! This special group represents the *élite* corps from which recruits for the traumatic etiology of diabetes should be most easily obtained, but that I have recognized none with a traumatic basis among the

TRAUMA AND DIABETES

more than 200 of this class I have personally studied, is of some import. One of the best examples in my own clientele of the sudden beginning of diabetes is the following:

Case No. 13,332, who was in perfect health, so far as he or his family knew, on December 24, 1934. That night, this 14-year-old Jewish boy, with diabetic heredity, slept without rising from bed. On Christmas day there was no especial excitement or careless eating, yet at night he rose six times, and 17 days later, when I first saw him, the urine contained eight per cent sugar. He was doing well in September, 1942, but the diabetes persists.

There was no accident here to cause diabetes. There was no heredity known at the time, although later it was learned his mother's cousin had diabetes. Suppose your automobile injured this lad while coasting on Christmas Day, or that for some reason you had severely reprimanded him and he had undergone an emotional reaction. I feel confident that abroad, if the case came into court, the acute onset of his diabetes would be put in evidence against you, and for social and insurance reasons he would have secured favorable consideration unless in a country where he would be debarred by race. In such a situation attention should be focused on the overwhelming number of similarly acute cases, which spring into being without any reason whatsoever to suspect physical or psychologic trauma. All these considerations, therefore, show how essential it is to investigate the background of any case of trauma in which diabetes may be a factor.

TRAUMA RARELY A DIRECT CAUSE OF DIABETES

Less and less credence has been given to the direct causation of diabetes by trauma since 1889, when it was demonstrated that its etiology and pathology centered in the pancreas. Total removal of the pancreas in a dog invariably brings on the disease, but that organ has such a high factor of safety that it fails to appear if more than one-fifth of the gland remains. This anatomic fact, in itself, shows how futile the attempt must be to connect bodily trauma with diabetes. Moreover, the pancreas lies in the depths of the abdominal cavity, with the abdominal wall, peritoneum and stomach in front of it, is partly overhung by the liver and in close touch with the spleen, and posteriorly is protected by the backbone. It is hardly conceivable that four-fifths of it could be destroyed and yet allow life to go on. The discovery that insulin, the hormone which controls the disease, is manufactured only in the *beta* cells of the islands of Langerhans scattered through the pancreas and weighing only one-twentieth that of the entire gland, made the evidence of the unity of diabetes complete.

Subsequently, the close connection of the pituitary gland, situated in its bony case in the center of the skull, with diabetes was recognized, and, later, it was found that actual diabetes could be brought on by injections of an extract of its anterior portion. At first, this reawakened the thought that the nervous system after all was independently involved in the causation of

diabetes and that diabetes was perhaps influenced both by functional as well as organic insults to the brain. Such suppositions, however, were soon dispelled when investigation disclosed that the diabetogenic action of the anterior pituitary extract lay in its power to destroy the cells of the pancreas which produce the insulin and thus caused the disease. Thereby the unity of diabetes and its localization in the pancreas was again demonstrated. (Very recently the influence of the suprarenal gland upon carbohydrate metabolism has received fresh emphasis.) An injection of the extract of its cortex will accentuate diabetes and, conversely, removal of the cortex will lessen its severity. In rats, Ingle has produced a diabetic state by injection of massive doses of cortical extract, but this does not persist when the injections are interrupted. Evidence regarding changes in the pancreas is as yet not available. I know of no instance in a human being in which disease or injury of the adrenal gland has brought on diabetes.

Today, to prove that trauma causes diabetes one must show that the pancreas is gravely injured, in fact, at least four-fifths destroyed, probably nine-tenths, or that the trauma has so acted upon the anterior pituitary gland as to cause it to discharge an excess of extract which, in turn, can destroy the insulin-producing cells of the pancreas. These are the two methods, but examples of the same are almost unknown in humans. For the pancreas, to my knowledge, there exist only the cases of Wells, Stern, and the two of Grafe, which have gained general recognition as proving injury to the pancreas led to diabetes, and not one of these cases is above criticism. As for trauma to the pituitary leading eventually to diabetes, the evidence is still less convincing, and Rathery's recent description of an acromegalic with a complicated head injury, is only remotely conceivable as an example of stimulation of pituitary remnants to excessive secretion. As a matter of fact, he did not attribute the diabetes in this acromegalic, following removal of an eosinophilic adenoma of the pituitary, to the pituitary itself, but rather to the injury of the neighboring hypothalamic region.

Grafe's case of trauma causing diabetes, in my opinion, is the most striking of any in the literature. A condensed report of it is herewith appended:

Grafe's Case.—A merchant, age 75, supposedly free from diabetes, *en route* to a bath cure on account of gallstones, while driving at 50 miles an hour, put on his brakes sharply to avoid a motorcycle and hit a tree. His chest and abdomen were pressed against the steering wheel. No pain followed the accident and he resumed driving, but within three hours developed a gallstone attack. Nevertheless, he continued his journey the next day with a hired chauffeur but, the attack persisting, transferred to a train. Upon arrival at the Spa two days after the accident, he was somnolent, had an acetone breath, showed blood in vomitus and stools and had marked thirst. The glycosuria was 4.7 per cent, blood sugar over 500 mg. Upon entrance to Grafe's Clinic that same day the breath had an acetone odor, glycosuria 4.5 per cent, marked reactions for acetone and diacetic acid, blood sugar 556 mg., no vomiting. There was pallor, pulse good, hemoglobin 85 per cent, abdomen perfectly soft, and although no pain on pressure, cautious palpation revealed indistinctly a sausage-shaped tumor. Glycosuria and acidosis were controlled during the night with 160 units of insulin but

TRAUMA AND DIABETES

although conscious in the morning with blood sugar 84 mg., he failed rapidly and died at 8:30 A.M. Autopsy showed thrombosis of the splenic vein with pancreatic apoplexy, thrombosis of a branch of the portal vein, fat necrosis of the omentum and mesentery, diffuse peritonitis, and general congestion of the organs.

Grafe's case would appear to show that an injury to the pancreas could be a direct cause of diabetes. However, I have not met with such an instance among the 22258 patients consulting me on account of sugar in the urine. Although his case fulfills many of the criteria essential to explain the onset of diabetes as the result of an accident, nevertheless, its deficiencies are plain: First, diabetes was supposedly absent but not proved absent before the accident. The age of the patient, his sedentary occupation, the association with gallstones, which so often are present in the obese, along with diabetes, raise grave doubts as to the development of diabetes *de novo*. Criticisms of this nature can be raised with nearly every case of so-called traumatic diabetes, but of course are not wholly valid. The case, however, is a model one in these respects because: First, an attempt was made to rule out the presence of diabetes before the accident; second, the accident was of an overwhelming nature to the abdominal region; third, the diabetes followed closely upon it; and, fourth, the autopsy disclosed an extreme injury to the entire pancreas. At the same time, it emphasizes how extraordinarily rare such an incident could occur and the patient live long enough to have diabetes.

Injury to the Pancreas without External Bodily Trauma.—The pancreas being the center around which diabetes revolves, any avenue of attack upon that organ, even indirectly due to trauma, must be considered. There are various possibilities.

Pancreatitis: This is not an uncommon condition. When an inflammation attacks the gland it is generally severe, extensive and serious, and usually results in death. Strange to say, pancreatitis is seldom accompanied by diabetes. I have had one case among my 22,258 diabetics in which it appeared to be of causal significance. Umber, in his series of 7,000 diabetics, reports one instance, and although others less well authenticated have been described, the total number of cases either in a series of diabetics or in a series of cases of pancreatitis is surprisingly small. Nevertheless, if trauma could be shown to produce pancreatitis there would be some ground for considering it as leading to diabetes. The gallbladder is so near the pancreas that the possibility of infections spreading from it into the pancreas causing diabetes appealed to me for many years. Statistical evidence based upon my own cases and upon studies of the Metropolitan Life Insurance Company forced me to give up this idea.

Hemochromatosis is a disorder of metabolism which leads to a deposition of iron pigment in various cells of the body. Usually it is accompanied by diabetes obviously brought about by deposition of the pigment in the cells of the islands of Langerhans of the pancreas which ultimately leads to their destruction. It was suggested by Mallory that the ingestion of copper was

the cause, but as yet that explanation has not been generally accepted. Conceivably, exposure to poisoning by copper or to anything which would bring about hemochromatosis might be adduced as trauma and thereby an indirect cause of diabetes.

Cancer involves the pancreas and exceptionally is accompanied by diabetes. It is not always easy to say which disease begins first, but there are a few instances in which the author reporting the case considered that the onset of cancer was first and diabetes followed. But if there is evidence that trauma can cause cancer of the pancreas, I do not know of it.

Infections: It is true that diabetes is occasionally discovered at the time of an infection, but infections are so frequent and the detection of diabetes so rare during them that statistical evidence pointing to cause and effect is slight. Priscilla White found in our diabetic children that the incidence of infections in the preceding history was distinctly less than the incidence of infections in children generally. Lande, writing from Umber's clinic, came to the same conclusion.

An infection makes an existing diabetes more severe is a statement commonly accepted, but there is, likewise, agreement that following the subsidence of the infection the type of the disease returns to its former level. Prolonged infection, whether due to the pyrogenic group of bacteria or to the tubercle bacillus, finally ceases to aggravate the diabetes, as my colleague, H. F. Root, has shown. The fundamental principle that an infection makes the diabetes worse is so generally accepted that it need not be further elaborated here.

Injuries to the Nervous System: Both psychical trauma and organic trauma to the nervous system have often been adduced as a cause of diabetes, but both were dissipated by the World War. Labbé, in France, did not consider trauma an etiologic factor in a single one of 600 diabetic soldiers. I was medical consultant at Mesves hospital centre, through which passed 38,765 soldiers, and there were but three cases of diabetes, two of whom I saw, and there was not the slightest indication that they were related to psychic or organic trauma. "Yet the World War presented an ideal opportunity for the physical and psychic traumatic origin of diabetes both in the combatants and noncombatants and that the disease did not materialize is most significant. The fear of an operation or of the pain incident to child-bearing and the extraction of teeth do not bring on diabetes, neither do we know, nor have we read in the literature, of a surgeon who postponed an operation for fear that the trauma incident to it would cause diabetes."

I know of no instance in which diabetes has been caused by accidents in the course of college athletics, particularly football. Dr. Arlie Bock, Department of Hygiene of Harvard University, wrote me in 1940: "As far as I can determine, no case of diabetes following trauma has occurred among athletes at Harvard. We have had many types of injury, but no known injury of the pancreas, and whether such trauma might result in diabetes I do not

know. You know there has been close medical supervision of athletes at Harvard for at least 25 years." A medical observer of pugilistic contests for 25 years assured me that he had never come across a single person who ever had any symptoms or any knowledge that he had diabetes or had been suffering from diabetes.

Dr. Harvey Cushing reported no instance of diabetes following the development of a tumor in the brain, save those in which diabetes occurred in connection with acromegaly and basophilism, and two patients (out of over 200) with chromophobe adenoma. "What is very significant," according to Dr. Louise Eisenhardt, "is that in Dr. Cushing's own long experience in operating for tumors of the hypophysis or third ventricle he found that such operations did not result in even a transient glycosuria." Dr. Gilbert Horrax, now in charge of the Neurosurgical Department of the Lahey Clinic, formerly Dr. Cushing's associate, confirms what Dr. Eisenhardt has written. Dr. Donald Munro of the Boston City Hospital writes: "I can cite the fact that, in over 3000 craniocerebral injuries, I know of no case in which the trauma had produced either diabetes mellitus or glycosuria by the time the patients had left the hospital after treatment for their injuries." In Germany, Jacobi quotes Liniger as reporting 300 severe head injuries without the development of diabetes and cites Bürger and Poppelreuter to the effect that among several thousand brain injuries no case of definitely traumatic diabetes was observed.

Opinions Pro and Con Trauma as a Direct Cause of Diabetes.—Viggo Thomsen, in his monograph of 416 pages, concludes: "Theoretically, it must be admitted that diabetes can appear as a direct sequel to a pancreas trauma which gives rise to extensive destruction of the pancreas. Other physical traumata are unable to cause diabetes. A physical trauma may give rise to an exacerbation of existing diabetes, but the exacerbation manifesting itself immediately after the trauma is temporary only. Thus the assertion frequently set forth that a physical trauma is able to exacerbate a latent diabetes so that the disease, owing to the trauma, becomes manifest cannot be maintained."

He reaches the above conclusions after an historical, clinical and experimental review of the subject. His conclusions are based, first, upon a study of 144 surgical accident cases admitted to the Aarhus District Hospital, in Denmark, to 100 of whom he gave a glucose tolerance test within three days after the accident. Of the 50 showing disturbances of carbohydrate metabolism, and discharged, he followed the course of 47 for periods of 6 to 38 months. Second, he investigated the effect of the accident on 100 injured diabetics. Third, he compared the antecedent history of trauma in 457 diabetics and a similar number of nondiabetics. "The results of this examination indicate that there is scarcely any difference in the frequency of occurrence of diabetes in injured and noninjured persons of the same age and standard of life." Finally, fourth, he summarizes the details of 81 cases of reported alleged diabetes in the literature.

Lommel, however, is a recent writer who takes up the other side of the question and presents it forcibly, citing the authors who support his view. He argues against rigid dogmatism in so complicated a condition as the causation of diabetes. His theme is that it is not right to assert that because a given explanation *ought not to be* correct is a reason that it *cannot be* the explanation. He assumes the cause of diabetes to be unknown and that it probably comes from an interrelation of many circumstances. He points out the paucity of changes in the pancreas in diabetic children, but he overlooks here, to my mind, the transitory nature of hydropic degeneration when diabetes first appears and the slow development of hyaline changes in the islands in the young. As for heredity, he considers this disposition to diabetes well-nigh universal. He does not believe in a sharp distinction between glycosuria and diabetes and thus is in definite antagonism to men, such as von Noorden, with large clinical experience. To some extent he concedes psychic trauma can lead to diabetes, but to this conclusion I suspect he is evidently somewhat influenced by Strieck's experiment on injury to the hypothalamic area, which has not yet been confirmed. On the other hand he demands (1) that the subject must be proved to be not obviously sick before the accident; (2) that the trauma must be severe, either acting externally with force or exerting a sudden, powerful, psychic provocation; (3) that the glycosuria shall be lasting; and (4) appear in not too remote a period from the accident.

Lommel, in writing his article, has evidently not been in touch with recent experimental work outside of Germany, which has so greatly clarified the problem of the causation of diabetes, and indeed his ideas are also contrary to the prevailing view in Germany itself when he wrote.

Troëll, in Stockholm, in a carefully prepared article, reports ten cases in which glycosuria or diabetes was present with trauma, and even passed upon by the board of reparations. In only two of these was the trauma considered as a cause of the diabetes. The evidence by no means was as strong as in Grafe's case and, in one, followed an injury to the elbow, and the *post hoc propter hoc* argument was raised because the urine was said to be sugar-free the day before the accident. In two instances temporary glycosuria followed a pistol shot wound of the chest or a fracture of the internal malleolus, in a fifth, the later entrance of cancer into the situation led to compensation, in two, trauma delayed, and in two, did not delay healing, and in fact the diabetes was directly responsible *per se*. The tenth, was a case of long duration in which the injury was insignificant and pneumonia decisive. These cases are carefully reported and the circumstances of each are clearly discussed. Troëll, like Lommel, is unwilling to concede that trauma to the pancreas alone can cause diabetes. He believes, as Naunyn emphasized, peripheral injury elsewhere *via* paths of the sympathetic nervous system could be a factor in bringing on the diabetes disagreeing

absolutely with Thomsen. His views seem to me to be biased by Swedish social accident insurance.*

THE ACTIVATION OF LATENT DIABETES BY TRAUMA

The presence of (1) heredity makes an individual susceptible to diabetes, and when to this we add (2) an age in which the incidence of diabetes is high, (3) obesity, (4) reduced exercise, and (5) an infection, the stage is set for a latent diabetes to become manifest. Such a situation is not unusual, and one of the commonest examples is the individual who develops a carbuncle following an almost infinitesimal trauma. With the fulminating carbuncle, the diabetes previously unrecognized, although very likely existent, according to Naunyn, may become critically severe, requiring 100 or more units of insulin, and yet when recovery ensues insulin can be omitted and the diabetes again becomes so submerged that the patient can tolerate more than 200 grams of carbohydrate and, to the unwary, appear cured. But the diabetes is still there, latent, ready to come to the surface again on any provocation. One must extend the importance of trauma far beyond the case of the man with a carbuncle. Any injury to an hereditarily predisposed individual, provided in its train come prevention of customary exercise, exposure to overeating, and particularly if an infection is involved, one must agree, makes a latent diabetes liable to become active. It is by no means necessary that all these factors be present. Proper treatment can control such a diabetes, which is usually mild and may make it appear nonexistent, but the disease once established is really not cured. Space does not allow the presentation of cases, but such have been already published by me. It is the indirect effect of the accident rather than the direct trauma which causes the trouble.

TRAUMA IN THE COURSE OF DIABETES

Trauma is very common in the career of a diabetic. We have 1800 or more diabetics at the New England Deaconess Hospital annually, in ward

* In this connection, a patient is recalled who had been himself an insurance salesman. He maintained in court action, directed against an insurance company, that he had sustained an accidental injury to one toe by stubbing it against a chair on a public excursion boat in Boston Harbor. This injury he claimed had led to infection, and the injury had resulted in diabetes followed by angina pectoris. It happened that he had a peculiar insurance policy which provided for triple indemnity in the event of injury occurring accidentally on a public carrier. If it could have been maintained successfully that this accident had caused not only the injury to the toe, but *via* the sympathetic nervous system, also the diabetes and angina pectoris, under the terms of his contract the total indemnity would have been about \$80,000. Actually, in this case the records showed that his diabetes had existed prior to the accident. If such an interpretation as the claimant urged had been accepted by the courts and a precedent thus established, it is easy to see that insurance premium rates would eventually be greatly increased either generally or specifically in patients where diabetes could be established from hereditary family history. Therefore, actually, the acceptance of such a point of view while probably immediately profitable to the one person involved would have social consequences for a large number of people, which would be most costly.

beds and private rooms. At various times, surveys have shown that 45 to 50 per cent of all our diabetic patients, under treatment at any one time in the hospital, came on account of an accident, but this statement is somewhat misleading. Such cases require a longer hospital stay and, therefore, appear proportionately more numerous than they actually are. It would be a fairer statement that one-quarter to one-third of all the patients in the Clinic in the course of a year represented the incidence of trauma. Accidents taking place in the hospital were found to occur relatively six times more frequently among the diabetics as among the nondiabetics. In statistics gathered from New York hospitals the incidence of operations upon the lower extremities in diabetic women was 150 times that in nondiabetic women. The diabetic is more susceptible to trauma than the nondiabetic, because his tissues are more vulnerable.

Purposely, in this discussion I will say little about those controversial features such as tissues of diabetics and the corresponding deficiency in glycogen. Such alterations cannot help affecting the soil, but it is difficult to measure the effect. In one instance we have the normal state and in the other an abnormal status, and that cannot be as advantageous. Then there are the abnormalities due to the products of acidosis; to excess of cholesterol; to an imbalance in the mineral constituents—all, very likely, are important in affecting the resistance of the part but not necessary to prove the diabetic more vulnerable to trauma, because there are so many other features in the diabetic which plainly influence the issue of the trauma for better or worse.

The degree of vulnerability varies with the age of the individual and his circulation, the nerve supply of the part, the severity of the diabetes, the duration of the disease, and its degree of control, not alone at the instant of the trauma, but from the day of onset of the diabetes.

Diabetics at present, based on mortality tables, are living about 14 years and approximately one-half die of arteriosclerosis in one or another of its various manifestations. Add to the developing arteriosclerosis in a diabetic the hardening of the arteries which comes to everyone as age advances, and his susceptibility to trauma increases. Arteriosclerosis implies deficient circulation, and circulation is all important in the healing of wounds. Step on the toes of a child or young adult and he forgets it in a few minutes, but the same blow on the foot of an old man may cause him to be confined to his bed for weeks, and, if a diabetic with poor circulation, he can lose his toe, his foot, his leg or even his life. The blow in one instance is on tissue with good circulation, in the other with poor circulation. On one side of the highway between Phoenix and Tucson the crops are flourishing, but on the other the land is barren and the irrigation canals, the circulation in the soil, show the reason why.

The normally functioning nerve supply of a tissue not only affects susceptibility to trauma, but the ability to heal the injured part. This is easily

overlooked. The wires are there, but they do not always transmit the messages or only a part of them. The diabetic may lose the sense of distinguishing between heat and cold and as with two of my patients the foot gets frost-bitten on Cape Cod or burned in Canada. His sense of pain is impaired and four of my patients have walked around at work all day and on removing their shoes at night found a tack which had evidently penetrated the sole of their foot hours before. My colleague, Howard F. Root, has collected 15 of our cases in which the ankle bones were actually destroyed and without the patients experiencing pain—a condition known as a neuropathic joint, akin to the Charcot joint of syphilis. I have seen a surgeon repeatedly open with strong scissors, in the ward before a group of visitors, nonnecrotic areas in diabetic feet for drainage or other reasons, making cuts one or two inches long without any anesthetic or any sign of discomfort on the face of the patient. It is seldom we do not have a patient with anesthetic feet in the hospital, and so vicarious is the absence of sensation that one foot may be anesthetic and the other not. I suspect that some of our patients who have gangrene originating from trivial exposures may have their lesions dependent upon lack of trophic nerve activity. Then there is the liability to accident because of loss of power due to the nonfunctioning of the motor fibers of the nerve. Common examples are toe-drop (peroneal paralysis), inability to rise from a chair (quadriceps paralysis) and double vision (external rectus), and, in rare instances, almost complete paralysis of the muscles of the entire body. Is it any wonder such people have accidents? The neuritis may affect the nerves of the intestines, resulting in an almost intractable diarrhea or those of the urinary bladder with distension and paralysis of that organ. In Walla Walla, Washington, just at the edge of the city, there are fields of luxuriantly growing onions and I was told the land was worth \$1000 an acre, but across the way the property looked the same to me, but was uncultivated simply because a mineral was lacking in the soil. Some diabetics are lacking in an efficient nerve supply.

The severity of the diabetes affects the vulnerability of the diabetic. His disease may be so mild that it is almost impossible to distinguish between health and diabetes, and this status may last for 10–20 years if moderate discretion in living is observed. Contrast this type with that of the severe diabetic who with exposure to extra exertion, directly incident to trauma, can go into coma. The liver of a mild diabetic is good enough to allow him to take ether, but give it to a severe diabetic, uncontrolled for the time being, and he dies of acidosis, just as Case No. 729 did, who took ether for a dental extraction on Tuesday and died on the following Friday of diabetic coma in preinsulin days. The severe diabetic is the one who has the complications affecting the circulatory and nervous systems, complications of the eyes with all that goes with impairment or loss of sight, and even complications of the bones in part due to their decalcification. This is manifest even in young patients. A review by Eisele of our 73 children, onset

under 15 years of age, who have survived 20 or more years of diabetes, illustrates the seriousness and frequency of complications in the diabetic which make him a prey to accidents. Thirty per cent of those examined roentgenologically showed peripheral arteriosclerosis, 55 per cent moderate to advanced arteriosclerosis, and 70 per cent of the patients showing these changes had either a high blood pressure or albuminuria, or both, at an average age of 29 years.

An infection makes a diabetes worse. To that all agree. The instant an infection enters the picture of trauma a whole train of disastrous consequences is set loose. The infection not only makes the diabetes more severe, but it usually prevents exercise, a most desirable adjunct to diet and insulin in the trilogy of treatment, confines the patient to bed, with the possibility of contracting pneumonia, bed sores, and, with the old, to disarrangement of life-long habits of regulating the action of the bowels and urinary tract, which in the end may prove to be far more serious than the accident itself.

The duration of the disease counts. How can it help it? Before the discovery of insulin, up to 1914, my patients lived 4.9 years, and 1.8 per cent survived 20 years. Today, fortunately, the average duration has lengthened to 14.3 years, and 19.1 per cent survive 20 years, and eight per cent over 25 years. They cease to live because they are more vulnerable. Their life expectancy was two-thirds, and I hope in the next series studied will be three-fourths that of their nondiabetic confrères. Although not always measurable, yet with each added year of a diabetic's life there is some impairment in bodily function.

Finally, the degree of control of the disease counts too. Insulin has proved that for the average diabetic. Even before insulin was discovered adherence to the diet and good hygiene enabled many a moderately severe diabetic in the older age-groups to live. Between 1922 and 1929 gangrene caused 8.5 per cent of our 1448 deaths, but between 1937 and 1940 only 4.7 per cent of 929 deaths. The duration of the disease was 8.1 years in the former period but was 12.5 years in the latter, the average age at death being, respectively, about 63 and 67 years. Thus, better control of the disease despite its longer duration and the older age of the patients reduced the mortality from gangrene which in about half our cases was provoked by trauma. The same degree of trauma can play havoc with a poorly controlled diabetic which would be tolerated with comparatively little trouble by a diabetic living up to the rules. Most of the difficulties of the diabetic are of his own choosing.

TRAUMA IN CONNECTION WITH THE USE OF INSULIN

Within a very few months after the use of insulin in human beings instances of infection at the site of injection of insulin ceased to occur. Among 1838 admissions to the George F. Baker Clinic during 1941 there were but 8 who entered for abscesses due to the injection of insulin. When one considers that only this small number of incidents occurred among many million injections in patients both inside and outside the hospital, it is evi-

TRAUMA AND DIABETES

dent both the manufacturers and the patients use care. Needles broken in the skin during injection have never led to serious trouble in my experience, and such occurrences are even more rare than abscesses. A far more frequent, and infinitely more serious, opportunity for trauma is that incident to an insulin reaction. However, despite the thousands of insulin reactions occurring in the course of treatment of diabetics, I do not remember one resulting in a fracture. This is in marked contrast to the incidence of fractures when insulin is employed to produce convulsions in nondiabetic neurologic patients. I did observe one case in which death appeared to result from the patient, while unconscious, having regurgitated food which plugged the trachea. Still more serious are those cases in which an insulin reaction has been mistaken for diabetic coma and, in consequence, a dose of insulin has been given which resulted in death. Fortunately, such instances are few, in fact, I know of but nine among 15,000 or more of my patients who have had insulin administered. Four of these received additional insulin while in shock, one, undoubtedly, took a lethal dose of insulin with design, and the circumstances regarding the remainder were somewhat obscure. None of the cases were observed in Boston, and but five were seen in consultation.

In the preparation of this article I have been aided by too many friends to mention here, but I am especially indebted to Dr. Howard F. Root, my colleague of 24 years, who not only has given detailed help but agrees with me in the views expressed.

INDEX

THE RELATION OF TRAUMA TO DIABETES

A—INTRODUCTION

1. Fundamental Facts Concerning Diabetes
2. Concepts Concerning Trauma and Diabetes

B—THE DISEASE DIABETES

1. Diagnosis
2. Did Diabetes Precede the Trauma?
 - (a) Incidence of diabetes
 - (b) Heredity in diabetes
 - (c) Obesity in diabetes
 - (d) The type of onset

C—TRAUMA RARELY A DIRECT CAUSE OF DIABETES

1. Grafe's Case
2. Injury to the Pancreas without External Bodily Trauma
 - (a) Pancreatitis
 - (b) Hemochromatosis
 - (c) Cancer
 - (d) The Rôle of infections
 - (e) Injuries to the nervous system
3. Opinions *Pro* and *Con* Trauma as a Direct Cause of Diabetes
 - (a) Thomsen
 - (b) Lommel
 - (c) Troëll

D—THE ACTIVATION OF LATENT DIABETES BY TRAUMA

E—TRAUMA IN THE COURSE OF DIABETES

F—TRAUMA IN CONNECTION WITH THE USE OF INSULIN

REFERENCES

- ¹ Joslin: Trauma and Diabetes in Trauma and Disease. 2nd. Ed., Brahdy, L., and Kahn, S., Eds., Philadelphia, Lea and Febiger, 1941, pp. 536-589.
- ² Joslin, Root, White and Marble: Treatment of Diabetes Mellitus. 7th Ed., Philadelphia, Lea and Febiger, 1940, pp. 76-87.
- ³ Konjetzny and Weiland: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 28, 860, 1915.
- ⁴ Timpe: Arch. f. Orthopäd. u. Unfall. Chir., 35, 112, 1935.
- ⁵ Wilder: Clinical Diabetes Mellitus and Hyperinsulinism. Philadelphia, W. B. Saunders Company, 1940.
- ⁶ Pincus and White: Personal communication. See also Brahdy and Kahn, loc. cit., p. 537.
- ⁷ Adams: In Joslin, Root, White and Marble, loc. cit.,² p. 61.
- ⁸ Ingle: Endocrinology, 31, 419, 1942.
- ⁹ Wells: Am. Jour. Med. Sci., 164, 479, 1922.
- ¹⁰ Stern: Am. Jour. Surg., 8, 58, 1930.
- ^{11a} Grafe: In Joslin, Root, White and Marble, loc. cit.,² p. 82.
- ^{11b} Grafe: Med. Klin., 34, 403, 1938; 34, 430, 1938.
- ¹² Rathery, Froment and Bargeton: Bull. et mem. Soc. méd. d. hôp. de Paris, 57, 114, 1941.
- ¹³ Umber: Med. Welt, 9, 889, 1935.
- ¹⁴ White: In Joslin, Root, White and Marble, loc. cit.²
- ¹⁵ Lande: Klin. Woch., 101, 359, 1931.
- ¹⁶ Labbé: Ann. de med. leg., 7, 541, 1927.
- ¹⁷ Bock: In Joslin, Root, White and Marble, loc. cit.,² p. 77.
- ¹⁸ Eisenhardt: In Joslin, Root, White and Marble, loc. cit.,² p. 77.
- ¹⁹ Horrax: In Joslin, Root, White and Marble, loc. cit.,² p. 77.
- ²⁰ Munro: New Eng. Jour. Med., 224, 766, 1941.
- ²¹ Jacobi: Monatschr. f. Unfallheilk., 47, 136, 1940.
- ²² Thomsen: Studies of Trauma and Carbohydrate Metabolism with Special Reference to the Existence of Traumatic Diabetes. Acta med. Scandin., Suppl. 91, 1938. (See also Editorial, Jour. Am. Med. Assn., 112, 1592, 1939.)
- ²³ Lommel: Med. Welt, 13, 836, 1939.
- ²⁴ Troëll: Der Chirurg., 12, 113, 1940.
- ²⁵ Naunyn: Der Diabetes Mellitus, 2nd Ed., Wien, Alfred Hölder, 1906, p. 139.
- ²⁶ Lisa, Magiday and Hart: Jour. Am. Med. Assn., 118, 1353, 1942.

ADDITIONAL RECENT REFERENCES

- Sano, M. E.: Am. Jour. Clin. Path., 11, 605-616, 1941.
 Le Melletier, J.: La Presse Med., 48, 620-621, 1940.
 Pedrazzini, F.: La Presse Med., 47, 707-708, 1939.
 Ferrabonc, Dubau and Bolot: Sc. méd. d. hôpitaux de Paris, 55, 1158-1162, 1939.
 Geiger and Benson: Am. Jour. Surg., 47, 672-674, 1940.
 Joslin, E. P.: Med. Clin. No. Am., 1213-1237, September, 1941.
 Root, H. F.: Med. Clin. No. Am., 441-447, March, 1937.

RELATION OF TRAUMA TO SYPHILIS OF THE NERVOUS SYSTEM

H. HOUSTON MERRITT, M.D., AND H. C. SOLOMON, M.D.

BOSTON, MASS.

FROM THE DEPARTMENT OF DISEASES OF THE NERVOUS SYSTEM, HARVARD MEDICAL SCHOOL; THE NEUROLOGICAL UNIT, BOSTON CITY HOSPITAL; AND THE BOSTON PSYCHOPATHIC HOSPITAL, BOSTON, MASS.

IN the light of our present knowledge of the pathology it may seem a little strange to discuss the rôle of trauma in the causation of syphilis of the nervous system. In the days before the discovery of the Wassermann reaction and the demonstration of spirochaetes in the brain and spinal cord of patients who had died of neurosyphilis, such a discussion would seem less out of place. Now that it has been proven that the signs and symptoms of neurosyphilis are due to the reaction of the body to the invading organism, the spirochaete, it would seem just as logical to discuss the rôle of trauma in the causation of scarlet fever or typhoid fever except for the fact that in most cases of neurosyphilis the onset of the signs and symptoms of involvement of the nervous system by the spirochaetes, may not appear for several or many years after the initial infection. During this interim the individual may be subjected to various influences, including trauma, which may be considered in certain instances to play a factor in the onset or progress of the symptoms. It is the purpose of this article to consider to what extent trauma can be considered of importance in the production or exaggeration of symptoms in the various types of neurosyphilis. It must be emphasized that in no case can trauma be considered as the sole or main cause of the signs or symptoms of syphilis of the nervous system. Our consideration must be limited to the evaluation of trauma as a secondary factor; whether trauma may cause changes in the nervous tissues which may make them more vulnerable to invasion by the spirochaete, or produce changes which will increase the number of symptoms or the progress of the disease in patients whose nervous system has already been invaded by these organisms. In addition to the severity of the injury, the time interval between the injury and the onset of symptoms is an important factor to be considered.

For clinical purposes cases of syphilis of the nervous system may be subdivided into three groups: 1. Meningeal, 2. Vascular. 3. Parenchymatous.

MENINGEAL NEUROSYPHILIS

In meningeal neurosyphilis the inflammatory process is confined to the coverings of the brain and the symptoms are due to irritation of these coverings and disturbance of function of the nerves which traverse them on the way to their exit from the skull or spinal canal. Thus, there are such symptoms as headache, nausea and vomiting together with disturbance of the function of one or more of the cranial nerves (paralysis of one-half

of the face, unilateral deafness, or paralysis of one or more of the muscles moving the eyeballs). Involvement of the meninges by syphilis usually occurs early in the course of the disease and it is common for the symptoms to have an acute onset within a few months of the appearance of the primary lesion. Occasionally the onset of symptoms may be delayed for many years after the infection. Since the symptoms may have a rather dramatic onset in this type of neurosyphilis, it is not strange that in an occasional patient such symptoms may appear to have a temporal relationship to some injury of a severe or trivial nature. It may be quite difficult in such cases to prove whether the injury has any relationship to the onset of the symptoms of meningitis. Several cases are reported in the literature in which the symptoms had their onset after a head injury. In a study of 80 cases of acute syphilitic meningitis which was made in 1935, we were unable to find any such coincidence. Since this report, however, we have seen two cases in which the onset of symptoms followed a head injury.

The first patient, a white male, age 27, was admitted to the hospital with complaint of severe right-sided headache and vomiting without nausea of five days' duration. Two days prior to the onset of symptoms he had been in a fight and had received a kick in the head but had not been rendered unconscious. There was a history of a penile chancre and a secondary skin rash six months previously. The neurologic examination was normal except for stiffness of the neck. The cerebrospinal fluid contained an excess of white blood cells and the Wassermann reaction was positive. The patient recovered rapidly with antisyphilitic treatment.

The second case was a white male, age 42, who was in an automobile accident in January, 1937. He was unconscious for an unknown interval and suffered a fracture of the leg. He was hospitalized for 11 weeks, during which time the cerebrospinal fluid was not examined. After discharge from the hospital he began to have severe headaches. These headaches continued and, in September, 1937, he began to have nausea and vomiting. He was readmitted to the hospital for study. The blood serologic tests were positive and the cerebrospinal fluid contained an excess of cells, and the Wassermann reaction was positive. The symptoms were rapidly relieved by antisyphilitic treatment.

In analyzing these two cases it would seem unlikely that the minor degree of trauma suffered by the individual in the first case cited above could have much relationship to the meningeal symptoms, since the time interval between the injury and the onset of the full-blown clinical picture was too short for the injury to have had any significant influence on the pathologic process. The situation is somewhat different in the second case where the injury was more severe and the interval between injury and appearance was such that it makes more tenable the hypothesis that the traumatic injury to the brain and meninges made these structures more vulnerable to the syphilitic infection.

In summary then, it may be stated that the incidence of syphilitic meningitis following head injury is an extremely rare occurrence. The burden of proof is, therefore, on the individual who tries to demonstrate such a relationship in any given case. Syphilitic meningitis is a relatively rare

TRAUMA AND NEUROSYPHILIS

clinical entity and, as stated above, usually has its onset in the first few months after the primary infection. An ideal case to prove the relationship of head injury to the development of syphilitic meningitis would have the following: 1. Primary infection several months before incurring a severe head injury. 2. Spinal fluid removed immediately after the injury showing no excess of white blood cells and negative serologic tests. 3. The development of symptoms one to eight months after such symptoms of an excess number of cells and positive serologic tests after the disease have developed. It is perhaps too much to ask for the complete fulfillment of all of these criteria and each case will have to be considered on its merits with particular regard to the number of criteria which it fulfills.

VASCULAR NEUROSYPHILIS

Involvement of the vessels of the nervous system by syphilis produce signs and symptoms similar to those developing in patients with disease of these vessels due to other causes, such as arteriosclerosis. Since the pathology of neurosyphilis is chiefly one causing a thickening of the vessels the mode of production of symptoms is more commonly due to an occlusion (thrombosis) of these vessels than a rupture. The signs and symptoms produced depend upon the location and size of the vessel involved. Such signs as hemiplegia, aphasia, hemianopia, *etc.*, are most commonly seen. In general, signs and symptoms of vascular neurosyphilis usually occur at two different stages of the infection. In the early stages of the disease, they may occur along with signs and symptoms indicating involvement of the meninges (syphilitic meningitis). At this time the vascular pathology is an occlusion of the vessels as a result of the inflammatory reaction in its outer sheath. In the later stages of the disease, proliferative changes (endarteritis) in the vessel lead to an occlusion. In only a few of such cases can the structural changes in the vessels be pathologically proven to be due to syphilis. In many cases the changes in the vessels are of such a nature that the pathologist is unable to state definitely the etiologic factors. This is particularly true when the affected individual is an elderly or middle-aged patient and also suffers from arteriosclerosis of a minor or severe degree.

The proof of the relationship of trauma to early vascular neurosyphilis is the same as that for the proof of syphilitic meningitis. In late vascular neurosyphilis the criteria for proof cannot be so definitely stated and should be the same as those for vascular lesions of any cause. It is commonly accepted that a severe injury to the head may be the cause of rupture or occlusion of vessels in patients with normal vessels and these are much more apt to happen in patients with arteriosclerotic vessels. It is logical to assume that such a trauma may have a similar effect on vessels damaged by syphilis. The following case is cited to illustrate the occurrence of symptoms after a head injury in a patient with presumed vascular neurosyphilis:

A colored female, age 37, was hit on the head by a baseball bat August 23, 1932. The skull was fractured and there was an injury to the right seventh nerve, with

complete paralysis of the fascial muscles on this side. Eighteen days later the patient fell to the floor unconscious while working in the kitchen. On recovery of consciousness there was a complete paralysis of the left arm and leg. The blood pressure was normal. Serologic tests of the blood were positive and there was an increase in the number of white cells and protein content of the cerebrospinal fluid.

In summary, it can be concluded that since trauma to the nervous system may damage normal vessels it is more likely to damage vessels already diseased by syphilis. The proof of causal relationship must rest upon an evaluation of the severity of the trauma and the interval between the trauma and onset of symptoms. Careful consideration must be given to the events connected with the presumed injury, since it may be possible that the onset of the vascular accident and resulting unconsciousness may be the cause of the so-called injury. For proof of causation it must be shown that: 1. The injury was *bona fide* and severe enough to damage nervous tissue. 2. That the symptoms had their onset immediately or within a reasonable interval after the injury.

PARENCHYMATOUS NEUROSYPHILIS

Involvement of the parenchyma of the brain usually takes the form of two well recognized syndromes: 1. Paretic neurosyphilis. 2. Tabetic neurosyphilis.

(1) *Paretic Neurosyphilis*.—Paretic neurosyphilis (dementia paralytica) is characterized pathologically by a diffuse encephalitis which is most intense in the frontal lobes of the brain. The clinical picture may be quite varied but personality changes and mental deterioration are prominent early symptoms. Convulsive seizures or transient neurologic signs, such as hemiplegia or aphasia, as well as any type of psychotic manifestation may be the initial sign of the disease. The interval between primary infection and development of symptoms is usually 10–20 years. The literature of 50 years ago contains considerable discussion as to the rôle of trauma in the production of paretic neurosyphilis but very little significance is given to this factor in modern literature, probably because the understanding of the disease makes the hypothesis of injury unnecessary. Pearce Bailey, in his classical treatise on Diseases of the Nervous System Resulting from Accident and Injury, in 1906, cites eight articles on the relationship of injury to paretic neurosyphilis. The authors cited by him gave the incidence of head injury in these patients as varying from 4.4 to 43 per cent. Bailey, himself, was skeptical of these reports and points out the difficulties in evaluating the rôle of trauma in the production of neurosyphilis, and states that in many cases the injury was a direct result of the disease itself (falls in convulsive or apoplectiform seizures or blows received in brawls precipitated by the psychotic behaviour of the individual), or the interval between the injury and the onset of symptoms was such that a causal relationship could not be considered tenable. The modern viewpoint, as expressed by such authors as S. A. K. Wilson and Kraepelin, tends to the view that if trauma

TRAUMA AND NEUROSYPHILIS

plays any rôle, it is quite a subsidiary one. Wilson states that the supposition is incapable of rigid proof that injury can evoke a morbid activity on the part of the treponeme which otherwise would not have been evidenced or that it can light up a latent process or intensify one already existent. He also states that there was no evidence of any such factors operating as result of head injuries in the first world war. Kraepelin states that in our present state of knowledge it is not possible to prove or disprove that an injury to the head has an unfavorable influence on a case of parietic neurosyphilis. Klauder and Solomon reviewed the subject in 1931, and it was stated: "That any conclusion as to the relation of cranial injury to a subsequently appearing dementia paralytica should not be reached solely on the length of time between the injury and appearance of the disease, but rather by correlation of the history antedating the injury; the nature of the injury; the character of the posttraumatic symptoms and their relation to the appearance of diagnostic symptoms of dementia paralytica."

The citation of several case histories where the development of symptoms followed a severe head injury may be of value:

Case 1.—A workman, who according to all accounts, was in perfectly normal physical and mental health, was blown through a double window in an explosion, badly bruising his head. A few weeks after the accident the patient began to show signs of mental disorder, performing foolish acts, showing evidences of memory loss, and finally becoming entirely unfit for work. Eight months later, examination in the hospital showed that the patient was confused, disoriented, and that he was given to foolish laughter. His judgment was greatly impaired and his memory was poor. There were signs of central nervous system disease, as indicated by reflex changes. The blood and spinal fluid examinations were typical of general paresis, which diagnosis was made.

Case 2.—A male, age 40, in apparently normal health, both physical and mental, was skating with a party of friends when he fell on the ice, striking his head a severe blow. He was rendered unconscious immediately. He was brought 60 miles to a hospital, and it was only after many hours that he began to regain consciousness. The clinical diagnosis was concussion with probability of subdural hematoma. A lumbar puncture was done which showed relatively little increase in pressure. While the matter of craniotomy was being discussed, examination of the spinal fluid gave the characteristic findings of general paresis. The patient never regained his normal mentality, requiring hospitalization in a mental institution, and despite antiluetic treatment has run the usual course of a parietic.

The judicial point of view can best be presented by abstracts from a Connecticut case designated in the legal parlance as "*Barry vs. Miller, et al.*," 104 Conn. 462; 133 Atl. 37 (1926)."

This was an appeal by the defendants from a finding and award of compensation in favor of the plaintiff. The appeal was dismissed.

Case 3.—The plaintiff, while working as a plasterer, stood upon a staging which fell, causing him to be thrown to the floor, a distance of about four feet, and to strike the floor in a sitting position. He was very pale, his eyes were closed, and he remained unconscious for from five to ten minutes, and upon regaining consciousness complained of pain in his back. He continued at work for about a month, complaining constantly of pain in his back, and in about ten days after the injury began to show

signs of nervous irritation and mental weakness. His nervous system and mentality were apparently normal before the injury. One and one-half months after the injury he was admitted to a hospital for the insane. While there he was found to be suffering from general paresis and that he had been suffering from syphilis many months prior to his fall.

The commissioner who heard the case found in Paragraph 13 that: "The injury of November 8, 1923, lighted up the syphilitic condition, and either caused or accelerated the onset of the paresis." The ground of appeal of the defendant is that this finding is made without evidence.

The Court, in its opinion, states as follows: "The evidence developed these further facts: The claimant had been, until the accident of November 8, in good health, physical as well as mental, and apparently with none of the objective or subjective symptoms of the disease paresis. The fall injured claimant's head slightly, as well as his back. When taken to the hospital on December 15, he was found to be suffering from acute paresis in an advanced stage caused by syphilis, it having existed for at least several months and causing him to become insane. Paresis is a chronic progressive disease. No cause for the onset of this acute form of paresis with which the claimant suffered following the fall was suggested by the two medical experts for the defendants, and none appears in the evidence unless the fall occasioned the onset.

"The experts for the defendants testified that this onset of paresis bore no relation to the fall, but they gave the commissioner no basis for this opinion other than that paresis was a germ disease and could not be caused by an injury either to the back or the head. The expert for the claimant testified that a latent disease such as paresis may be precipitated by an injury and that the injury which the claimant had suffered was sufficient to have precipitated this onset of paresis. This expert testified that he could not state positively that the injury precipitated this onset of paresis, but that it might have been accelerated by the fall or any shock to the nervous system; that if the claimant had not symptoms of paresis prior to the fall, and the symptoms of paresis developed immediately afterward—and that was true in this case—it was an exciting cause. This opinion he qualified by saying it might have been an exciting cause. In response to the commissioner's question, 'What are the probabilities or aren't there any?' he replied, 'I think that the probabilities are that anybody suffering with a disease, any kind of a chronic disease, chronic kidney trouble, or chronic lung trouble, any sudden shock to the nervous system, or shock to the body, especially with some disease of the nervous system, a sudden shock to the body would be apt to precipitate the disease, make it break out quickly.' The opinion of this expert, who testified as defendant's two experts had testified, was not later attacked or questioned by either of them.

"In this condition of the evidence, we cannot hold that the commissioner erred in finding that the injury precipitated the onset of the paresis. The commissioner might reasonably have found that the injury not only might have been, but that it probably was the occasion of this onset. The onset of a chronically progressive disease came upon the claimant, a man apparently well, physically and mentally, without a symptom or warning of its presence. There was no other cause suggested in the evidence. It was not only a possible but a reasonably probable cause. If the commissioner concluded from his evidence that the injury was a reasonably probable cause of the onset, it was his duty to find as a fact, as he has found that it did cause or accelerate the onset of the paresis."

From these records there is medical evidence and judicial precedent to connect trauma to the head with the development or acceleration of the paretic process. From a pathologic viewpoint it is important that a suitable interval elapse between the injury and the development of symptoms. In

TRAUMA AND NEUROSYPHILIS

the cases cited above, the injury could be sufficiently severe to cause damage to the nervous system and in the first and third cases the interval between the injury and the appearance of symptoms was sufficiently long for any deleterious effect of the injury to have influenced the paretic process. In the second case, the interval appears too short for such an effect. Similarly, appearance of symptoms after an interval of several years would hardly be appropriate. In general, the limits set by most authorities for a causal relationship between head trauma and the development of paretic symptoms as a minimum is six weeks to three months and as a maximum, two to three years. It is also logical to assume from the medical viewpoint that injuries to other parts of the body than the head can have no causal relationship to the development of paretic neurosyphilis nor can such factors as emotional shock be considered of any importance.

(2) *Tabetic Neurosyphilis*.—The situation with regard to tabetic neurosyphilis is analogous to that of paretic neurosyphilis, as discussed above. Pathologically, the two conditions are similar in that the primary involvement is in the parenchymatous tissues of the nervous system and there is a long latent period between the initial infection and the appearance of symptoms. The main difference between the two conditions is that in paretic neurosyphilis they are in the cerebral cortex, whereas in tabetic neurosyphilis they are in the spinal cord and midbrain. The symptoms of tabetic neurosyphilis are quite varied but the most common are: Lancinating pain in the body and extremities, disturbance of gait, loss of control of the urinary bladder, double vision from palsy of the eye muscles, atrophy of the optic nerves, visceral pains, trophic ulcers and degenerative changes in the joints.

The problem here, as in all cases of neurosyphilis, is one of precipitation or exaggeration of symptoms. Logically, it would seem necessary that the injury involve the spine to be a factor in evoking the spinal symptoms or to the head for the midbrain symptoms of tabetic neurosyphilis.

A case illustrating the development of symptoms of tabetic neurosyphilis after an injury can be cited:

A vigorous male, age 63, who claimed to have been perfectly well and enjoying the best of health, while playing a game of polo received an injury to his head which did not unseat him from his horse but caused him to feel rather badly. A swelling developed on the back of his head from the blow and he suffered pain in the back of the head and neck. There was no loss of consciousness. He complained subsequently of headache and dizziness. The next morning he got up and went out of the house but felt dizzy and had so much headache he stayed at home most of the day, although not requiring bed care. The following day he developed a diplopia which did not improve and which was present three and one-half years later. Examination at that time showed weakness of both external recti, absent knee jerks and positive serology. The case came to legal action, the plaintiff claiming that although the patient had tabes, the disabling symptoms were the result of a blow he received. Expert opinion differed. The defendant's neurologist stated that a blow that did not lead to unconsciousness would not start up a dormant syphilitic condition and make this condition active. He

further stated that the effect of such a blow would be the same whether the victim were syphilitic or nonsyphilitic. A second expert testified for the defendant that: "It is possible but not probable that a dormant syphilitic condition can be excited into action by a blow on the head that does not result in unconsciousness or fracture of the skull." He recognizes, however, that many authorities hold the opinion that such a result is probable, even though there be no fracture of the skull and no lacerations of the scalp, there may yet occur multiple hemorrhages in the deeper structures of the brain. It was this expert's opinion, however, that, taking into consideration the lack of severity of the blow, the symptoms which occurred were due solely to syphilis and developed entirely independently of any blow.

The expert testifying for the plaintiff held the opinion that a man, age 63, who had no active signs of tabes, would probably not develop such signs unless there was some exciting cause, such as a blow on the head, and that this need not be of great severity to cause the symptoms.

The decision rendered by the court was quite revealing. It was found that medical science could not determine with certainty the results which may come to any one from an injury to his head, and in such cases the decisions and opinions of physicians are not a matter of absolute certainty but are a matter of delicate clinical judgment based upon experience. It was decided that the symptoms, as described, could be explained adequately on the basis of syphilis alone, but the vital point in the given case is whether syphilis alone was responsible or whether the blow caused the development of the disease which otherwise would have given the patient no trouble. The final decision was that the blow was the immediate precipitating cause of the symptoms and the individual, therefore, was compensable.

The relation of the trauma and syphilitic arthropathies, or Charcot joints, affords less opportunity for a divergence of opinion. It is rather generally accepted today that Charcot joints develop as the result of lessened sensitivity in the joints which allow repeated minor traumata to occur without adequate protection by the muscles or tendons. In other words, the usual Charcot joint is traumatic, in the final analysis, in a patient with a defective sensory system. Numerous cases have been placed in the literature showing that trauma was the immediate cause of the development of the syphilitic arthropathy.

The defense of the hypothesis that external trauma can have an unfavorable influence on the tabetic process must be along the lines given above for parietic neurosyphilis. Direct trauma to the spinal cord by the injection of foreign substances into the spinal subarachnoid space (such as spinal anesthesia) while an extremely rare occurrence, may have a deleterious effect on the tabetic process, as illustrated by the following case, which also emphasizes the importance of an adequate examination of every patient before the administration of drugs intraspinaly:

A middle-aged white male, who had been previously in good health, was admitted to the hospital for the excision of external hemorrhoids. The records do not indicate that any neurologic examination or serologic tests were made before the administration of spinal anesthesia for the performance of the operation. After the operation the patient was unable to void his urine and there was weakness of the lower extremities. Neurologic examination showed the typical findings of tabetic neurosyphilis, and the cerebrospinal fluid, examined on numerous occasions, contained an excess of cells, an

TRAUMA AND NEUROSYPHILIS

abnormal colloidal gold test, and the serologic tests were positive in the blood and cerebrospinal fluid. There was gradual improvement of the patient's symptoms during the course of the next few years, during which time he received antisyphilitic treatment.

SUMMARY

The rôle of trauma in the precipitation or aggravation of the symptoms of neurosyphilis has not been adequately established on a scientific basis. The one proven fact is that neurosyphilis is due to the invasion of the nervous system by the spirochaete. The deleterious effect of trauma on the pathologic processes of neurosyphilis can only be deduced. There is divergence of opinion as to severity of injury and the appearance of symptoms. Since there elapse between the injury and the appearance of symptoms, it is the duty of the medical expert to keep within the limits of what is reasonable and not give the dignity of probability to conclusions that may only be considered as remotely possible. Likewise, it behooves the judiciary, granting that where there is reasonable doubt, the benefit of doubt should accrue to the victim, not to go too far in relating injuries to other parts of the body than the nervous system to the development of neurosyphilis.

REFERENCES

- ¹ Merritt, H. Houston, and Moore, Merrill: Acute Syphilitic Meningitis. *Medicine*, 14, 119, 1935.
- ² Bailey, Pearce: Diseases of the Nervous System Resulting from Accident and Injury. 1906. D. Appleton, New York.
- ³ Wilson, S. A. K.: *Neurology*, 1940. Williams & Wilkins, Baltimore.
- ⁴ Kraepelin, E., and Lange, J.: *Psychiatric*, 1927, Barth, Leipsig.
- ⁵ Klauder, J. V., and Solomon, H. C.: Trauma and Dementia Paralytica. *J. A. M. A.*, 96, 1, 1931.

READING LIST OF ENTIRE GROUP OF MEDICOLEGAL ARTICLES APPEARING CONCURRENTLY IN MEDICAL AND LEGAL JOURNALS UNDER EDITORSHIP OF DR. HUBERT W. SMITH

EDITOR'S NOTE: *The articles in this ANNALS OF SURGERY symposium are part of a series on Medicolegal subjects appearing simultaneously in many other medical and legal journals. The series is sponsored by Harvard Medical School Department of Legal Medicine and is under the editorship of Dr. Hubert W. Smith, of Harvard.*

JOURNALS

MEDICAL JOURNALS

1. Americal Journal of Psychiatry (Am. J. Psychiat.); 111 St. George Street, Toronto, Canada; price \$1.75 a copy.
- *2. Annals of Internal Medicine (Ann. Int. Med.); Green and Redwood Streets, Baltimore, Maryland.
3. Annals of Surgery (ANNALS OF SURGERY); East Washington Square, Philadelphia, Pennsylvania; price \$2.00 a copy.
- *4. Clinics; East Washington Square, Philadelphia, Pennsylvania; price \$2.00 a copy.
5. Medicine; Johns Hopkins Hospital, Baltimore, Maryland; price \$1.50 a copy.

LEGAL JOURNALS

- *1. Boston University Law Review (B. U. L. Rev.); 11 Ashburton Place, Boston, Massachusetts; price \$.70 a copy.
2. California Law Review (Calif. L. Rev.); Boalt Hall of Law, Berkeley, California; price \$.90 a copy.
3. Harvard Law Review (Harv. L. Rev.); Harvard Law School, Cambridge, Massachusetts; price \$.85 a copy.
4. Indiana Law Journal (Ind. L. J.); 38 Maxwell Hall, Bloomington, Indiana; price \$.75 a copy.
5. Michigan Law Review (Mich. L. Rev.); Hutchins Hall, Ann Arbor, Michigan; price \$.80 a copy.
6. North Carolina Law Review (N. C. L. Rev.); University of North Carolina, Chapel Hill, N. C.; price \$.80 a copy.
- *7. Rocky Mountain Law Review (Rocky Mt. L. Rev.); University of Colorado Law School, Boulder, Colorado; price \$1.00 a copy.
- *8. Southern California Law Review (So. Calif. L. Rev.); University Park, Los Angeles, California; price \$1.00 a copy.
9. Tennessee Law Review (Tenn. L. Rev.); 720 West Main Avenue, Knoxville, Tennessee; price \$.75 a copy.
- *10. University of Chicago Law Review (U. of Chi. L. Rev.); Chicago, Ill.; price \$.75 a copy.
- *11. Virginia Law Review (Va. L. Rev.); Clark Memorial Hall, Charlottesville, Virginia; price \$1.00 a copy.
12. Yale Law Journal (Yale L. J.); Yale Station, New Haven, Connecticut; price \$.80 a copy.

* Devoting entire April 1943 issue to the Symposium.

TITLES

I. PROJECTION PAPER

- (1) Smith, Hubert Winston: Scientific Proof and Relations of Law and Medicine, Ann. Int. Med., April, 1943; Clinics, April, 1943; B. U. L. Rev., April, 1943; Rocky Mt. L. Rev., April, 1943; So. Calif. L. Rev., April, 1943; U. of Chi. L. Rev., April, 1943; Va. L. Rev., April, 1943; Yale L. J., May, 1943.

READING LIST

II. CLINICAL FORENSIC MEDICINE

- (2) Brahdy, Leopold, and Samuel Kahn: Clinical Approach to Alleged Traumatic Disease, *Ann. Int. Med.*, April, 1943; *B. U. L. Rev.*, April, 1943.
- (3) Moritz Alan Richards: The Mechanisms of Head Injury, *ANNALS OF SURGERY*, April, 1943; *B. U. L. Rev.*, April, 1943.
- (4) Denny-Brown, Derek Ernest: Factors of Importance in Head Injury—A General Survey, *Clinics*, April, 1943; *Va. L. Rev.*, April, 1943.
- (5) Munro, Donald: The Late Effects of Craniocerebral Injuries—A Consideration of the Criteria Necessary to Evaluate the Possible Causes, *ANNALS OF SURGERY*, April, 1943; *B. U. L. Rev.*, April, 1943.
- (6) Solomon, Harry C., and Hubert Winston Smith: Traumatic Neuroses in Court, *Am. J. Psychiat.*, May-June, 1943; *Va. L. Rev.*, Summer, 1943; *Am. J. Psychiat.*, May-June, 1943.
- (7) Ebaugh, Lt. Col. Franklin G., and Major Henry W. Brosin: Traumatic Psychoses, *Ann. Int. Med.*, April, 1943.
- (8) Cobb, Stanley and Hubert Winston Smith: Relation of Emotions to Injury and Disease—A Call for Forensic Psychosomatic Medicine, *Ann. Int. Med.*, August, 1943; *Harvard L. Rev.*, Summer, 1943.
- (9) Merritt, H. Houston, and Harry C. Solomon: Relation of Trauma to Syphilis of the Nervous System, *ANNALS OF SURGERY*, April, 1943; *B. U. L. Rev.*, April, 1943.
- (10) Pollock, Lewis J.: Examination of Motor and Sensory Function as Related to Opinion Evidence, *Clinics*, April, 1943.
- (11) Marble, Henry C.: The Physician and the Workmen's Compensation Law, *Clinics*, April, 1943.
- (12) Schwartz, Louis: Problems of Proof in Claims for Recovery for Dermatitis, *Ann. Int. Med.*, April, 1943; *Mich. L. Rev.*, April, 1943.
- (13) Homans, John: Circulatory Deficiency in the Extremities in Relation to Medico-Legal Problems, *Ann. Int. Med.*, April, 1943; *N. C. L. Rev.*, April, 1943.
- (14) Bennett, Granville Allison: Medical Criteria Which Govern Relations of Trauma to Joint Disease, *Clinics*, April, 1943.
- (15) Smith, Hubert Winston, and Granville Allison Bennett: Joint Disease in the Courts: Select Problems of Proof, *Tenn. L. Rev.*, Dec., 1943.
- (16) Ober Frank Roberts: Some Practical Criteria for Use in Forensic Orthopedic Cases, *Clinics*, April, 1943; *Rocky Mt. L. Rev.*, April, 1943.
- (17) Aldrich, Robert Henry: Forensic Aspects of Burns, with Special Reference to Appraisal of Terminal Disability, *Va. L. Rev.*, April, 1943; *ANNALS OF SURGERY*, April, 1943.
- (18) Hertig, Arthur Tremain, and Walter Herman Sheldon: Minimum Criteria Required to Prove Prima Facie Case of Traumatic Abortion or Miscarriage, *ANNALS OF SURGERY*, April, 1943; *Rocky Mt. L. Rev.*, April, 1943.
- (19) Joslin, Elliott P.: Relation of Trauma to Diabetes, *ANNALS OF SURGERY*, April, 1943; *Rocky Mt. L. Rev.*, April, 1943.
- (20) Warren, Shields: Minimum Criteria Required to Prove Causation of Traumatic or Occupational Neoplasms (Cancer), *ANNALS OF SURGERY*, April, 1943; *U. of Chi. L. Rev.*, April, 1943.
- (21) Wolff, Harold G., James D. Hardy, and Helen Goodell: The Pain Threshold in Man, *Am. J. Psychiat.*, March-April, 1943.

III. FORENSIC PATHOLOGY

- (22) Leary, Timothy: How a Modern Medical Examiner's Office Functions in a Typical Investigation of "Sudden Death"; Points of Superiority over Coroner's Office, *Ann. Int. Med.*, July, 1943.
- (23) Jetter, Walter W.: When Can It Be Said That Death May Be Caused or Contributed to by Acute Alcoholism, *Clinics*, April, 1943.

IV. SCIENTIFIC CRIME DETECTION

- (24) Hoover, J. Edgar: The Scientific Crime Detection Laboratory, *Clinics*, April, 1943; *U. of Chi. L. Rev.*, April, 1943.
- (25) Wigmore, John H.: Circumstantial Evidence in Poison Cases, *Clinics*, April, 1943; *B. U. L. Rev.*, April, 1943.
- (26) Walker, Joseph: Scientific Evidence in Poisoning Cases, *Clinics*, April, 1943; *B. U. L. Rev.*, April, 1943.

V. MODES AND MECHANISMS OF SCIENTIFIC PROOF

- (27) Donaldson, Samuel W.: Medical Facts That Can or Cannot Be Proved by X-Ray: Historical Review and Present Possibilities, *Ann. Int. Med.*, April, 1943; *Mich. L. Rev.*, April, 1943.
- (28) Riseman, Joseph E. F.: Principles of Electrocardiography, *Rocky Mt. L. Rev.*, April, 1943; to be submitted for medical publication.

- (29) Smith, Hubert Winston, and Joseph E. F. Riseman: Applied Use of the Electrocardiogram in Legal Proceedings, Rocky Mt. L. Rev., April, 1943; Ann. Int. Med., July, 1943.
- (30) Snyder, Lemoyne M.: Criminal Interrogation with the Lie Detector, Rocky Mt. L. Rev., April, 1943; Ann. Int. Med., April, 1943.
- (31) Boyd, William: Protecting the Evidentiary Value of Blood Group Determinations, Clinics, April, 1943; So. Calif. L. Rev., March, 1943.
- (32) Maguire, John M.: A Survey of Blood Group Decisions and Legislation in the American Law of Evidence, Clinics, April, 1943; So. Calif. L. Rev., March, 1943.
- (33) Schoch, Magdalena: Determination of Paternity by Blood Grouping Tests: The European Experience, Clinics, April, 1943; So. Calif. L. Rev., March, 1943.
- (34) Ladd, Major Mason, and Robert B. Gibson: Legal-Medical Aspects of Blood Tests to Determine Intoxication, Ann. Int. Med., April, 1943; Va. L. Rev., April, 1943.

VI. SCIENTIFIC PROOF AS A MEANS OF TESTING PREMISES UNDERLYING LEGISLATION OR LEGAL DOCTRINE

- (35) Rock, John: The Scientific Case Against Rigid Legal Restrictions on Medical Birth-Control Advice, Clinics, April, 1943.
- (36) Myerson, Abraham: Certain Medical and Legal Phases of Eugenic Sterilization, Ann. Int. Med., April, 1943; Yale L. J., April, 1943.

VII. MEDICAL CRIMINOLOGY

- (37) Lennox, William Gordon: Amnesia Real and Feigned, Am. J. Psychiat., March-April, 1943; U. of Chi. L. Rev., April, 1943.

VIII. SOCIO-MEDICO-LEGAL PROBLEMS

- (38) Stearns, Commander A. Warren: Medical and Social Factors in Crime, Ann. Int. Med., April, 1943; Ind. L. J., July, 1943.

IX. SCIENTIFIC LEGAL-MEDICAL CORRELATIONS

- (39) Hooton, Earnest Albert: Medico-Legal Aspects of Anthropology, Clinics, April, 1943; Rocky Mt. L. Rev., April, 1943.

X. HISTORICAL NOTES ON LAW-SCIENCE RELATIONS

- (40) Thayer, James B.: Note on Poison in Roman Private Law, Clinics, April, 1943; B. U. L. Rev., April, 1943.
- (41) Polsky, Samuel and Spencer Bercsford: Some Probative Aspects of the Early Germanic Codes, Carolina and Bambergensis, Ann. Int. Med., May, 1943; B. U. L. Rev., April, 1943.
- (42) Simboli, David: Medico-Legal Vignettes, Clinics, April, 1943.

XI. EXPERT TESTIMONY AND JURIDICAL MECHANISM

- (43) Morgan, Edmund M.: Suggested Remedy for Obstructions to Expert Testimony by Rules of Evidence, Clinics, April, 1943; U. of Chi. L. Rev., April, 1943.
- (44) Pound, Roscoe: A Ministry of Justice as a Means of Making Progress in Medicine Available for Courts and Legislatures, Clinics, April, 1943; U. of Chi. L. Rev., April, 1943.
- (45) Chafee, Zechariah, Jr.: Privileged Communications: Is Justice Served or Obstructed by Closing the Doctor's Mouth on the Witness Stand? Ann. Int. Med., April, 1943; Yale L. J., April, 1943.

XII. PRIVATE LAW PROBLEMS OF INTEREST TO MEDICAL MEN

- (46) Dodd, Edwin Merrick, Jr.: Contracts Not to Practice Medicine, Ann. Int. Med., April, 1943; B. U. L. Rev., April, 1943.
- (47) Scott, Austin Wakeman: Tort Liability of Hospitals, Ann. Int. Med., April, 1943; Tenn. L. Rev., April, 1943.
- (48) Ludlam, Warren: Plaintiff's Duty to Minimize Defendant's Liability by Surgery, Tenn. L. Rev., April, 1943; to be submitted for medical publication.
- (49) Smith, Hubert Winston: Legal Responsibility for Non-Therapeutic Surgery, to be submitted for medical publication.
- (50) McCurdy, William Edward: Insanity as a Ground for Annulment or Divorce in English and American Law, Am. J. Psychiat., May-June, 1943; Va. L. Rev., April, 1943.
- (51) Arthur, William R.: Some Legal Aspects of the Use of Drugs (Tentative title), Rocky Mt. L. Rev., April, 1943; to be submitted for medical publication.

XIII. PUBLIC LAW PROBLEMS OF THE MEDICAL PROFESSION

- (52) Powell, Thomas Reed: Compulsory Vaccination and Sterilization: Constitutional Aspects, Ann. Int. Med., April, 1943; N. C. L. Rev., April, 1943.
- (53) Griswold, Erwin N.: The Doctor's Federal Taxes, Ann. Int. Med., April, 1943; Calif. L. Rev., June, 1943.

BRIEF COMMUNICATIONS

HYDROMETROCOLPOS IN INFANCY

CASE REPORT

MILLARD S. ROSENBLATT, M.D., AND PAUL V. WOOLLEY, JR., M.D.

PORTLAND, OREGON

FROM THE DOERNBECHER MEMORIAL HOSPITAL, AND THE DEPARTMENT OF SURGERY AND PEDIATRICS,
UNIVERSITY OF OREGON MEDICAL SCHOOL AND CLINICS, PORTLAND, OREGON

CONGENITAL ATRESIA of the vagina, when coexistent with abnormal activity of uterine and cervical glands, results in distension of the uterus and vagina proximal to the point of obstruction. Mahoney and Chamberlain¹ have recently called attention to the importance of this condition, hydro-metrocolpos, as the cause of palpable abdominal tumors in female infants, and have stressed the need for recognition of the complex before unnecessary and dangerous abdominal surgery is undertaken. They have pointed out that absolute diagnosis can be obtained in a suspected case through roentgenoscopic studies after the injection of radiopaque substances through the point of atresia. The logical treatment, incision through the imperforate membrane, resulted in complete regression of signs and symptoms in the single case where a correct diagnosis was made preoperatively.

We have recently had the opportunity to study a classic example of hydro-metrocolpos which afforded confirmation of the value of roentgenoscopy in establishing a correct diagnosis and illustrated the importance of acute urinary retention as a complicating factor.

Case Report.—Hosp. No. 127642: The infant, a female, age 17 days, had progressed well for the first few days following an uneventful birth. A progressive increase in the size of the abdomen was noted thereafter, and for several days prior to admission the output of urine had been reduced. The baby screamed constantly as if in pain. Examination showed her to be an adequate newborn. Her abdomen was markedly distended by a mass which extended from under the pubis to a point within three centimeters of the xiphoid. It was rounded, smooth, flat to percussion, and it did not present in the flanks. Presenting at the vagina was a smooth cystic mass which protruded when the baby cried but was not under the same tension as was the abdominal mass. Catheterization yielded 360 cc. of cloudy urine, and resulted in disappearance of the prominent abdominal mass, but revealed a second tumor in the midline, which was the size of a small orange, and, when felt through the rectum, was found to extend into the pelvis and to be confluent with the protuberance present at the vaginal outlet.

Procedure.—A needle was passed into the vaginal portion of the tumor and 30 cc. of mucinous grey fluid was removed and replaced by 20 cc. of radiopaque media. Roentgenograms then demonstrated the tumor to consist of a greatly dilated vagina and uterus (Fig. 1). A cruciform incision was placed through the vaginal protuberance and six ounces of fluid, similar to that aspirated, was allowed to escape, with almost immediate disappearance of the mass. A small amount of fluid continued to leak from the incision for a few hours and thereafter no discharge of any description was evident.

The postoperative course was complicated by pyuria and other evidences of an atonic bladder. Improvement was gradual over a period of two weeks, during which time frequent catheterizations were done and adequate chemotherapy was given. When seen at the age of three months the urine was clear and there was no bladder residual. The point of incision could not be made out at the introitus but there appeared to be a dilated hymenal ring which was free from tabs or other irregularities.

Whether this case is representative of an imperforate hymen or of actual atresia of the vagina has not been answered. Certainly, the protuberance appeared to descend from well above the usual site of the hymen and its wall was rather thick and vascular; suggesting more of an atresia. The fluid obtained by needling was similar in appearance to that so frequently noted in the normal newborn female. It was viscid, free from cellular elements, and contained 1.6 grams per cent of protein.



FIG 1.—Roentgenogram following replacement of contents of tumor with radiopaque media.

SUMMARY

A case of hydrometrocolpos, occurring in a newborn girl and complicated by acute urinary retention, is described. Such cases appear to depend upon the concomitant existence of an atresia of the vagina and an excessive secretion of cervical and uterine glands. A correct diagnosis can be established by visualization of the tumor after injection with radiopaque substance, and treatment is confined to incision through the atretic membrane. The true nature of the condition must be recognized, otherwise dangerous, crippling, and unnecessary abdominal surgery may be inadvertently undertaken.

REFERENCE

- 1 Mahoney, P. J., and Chamberlain, J. W.: Hydrometrocolpos in Infancy. *Jour. Pediat.* 17, 772, 1940.

AN IMPROVED TOWEL CLIP

JAMES B. BLODGETT, M.D.
BOSTON, MASS.

FROM THE LABORATORY FOR SURGICAL RESEARCH, HARVARD MEDICAL SCHOOL, AND THE SURGICAL CLINIC, PETER BENT BRIGHAM HOSPITAL, BOSTON, MASS.

A TOWEL CLIP designed to meet the defects of the usual clips has been used with satisfaction for the past year at the Peter Bent Brigham Hospital. There are two defects in the functional design of the ordinary towel

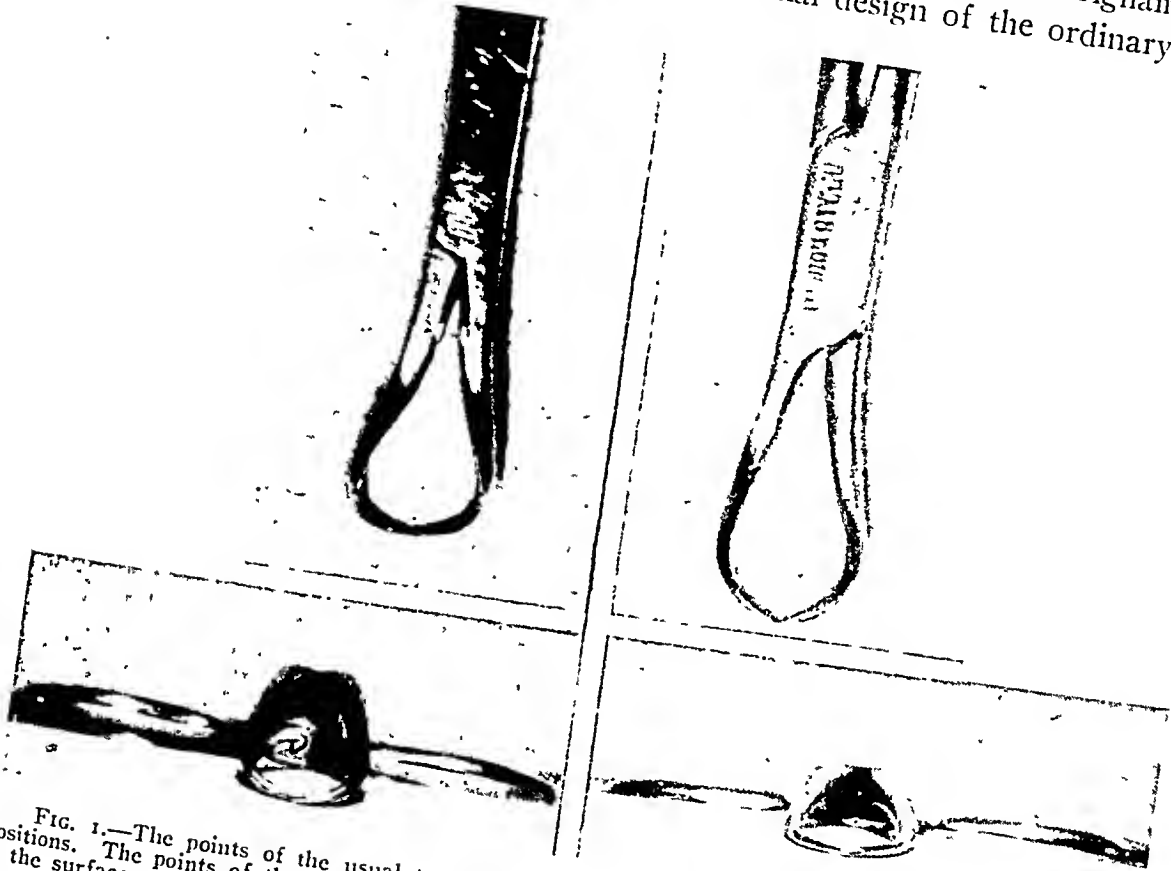


FIG. 1.—The points of the usual towel clip (left) are in the same relation to the surface in all positions. The points of the improved clip (right) point into the skin when it is held at right angles to the surface. When the clip rests on the skin below, the points are tangential, as in the older clip.

clip: First, it is difficult, or impossible, to make the points take a small bite into the skin through a towel, especially if the skin is on stretch, as in the scalp. This is because the points are essentially parallel to the skin surface in all positions of the clip, and the skin, therefore, must be "pinched" into the points before it is perforated. The second defect is that the slope or rise from the tips of the instrument to the box is so marked that the towel clip, in place at the edge of the incision, may interfere with other instruments used in the wound.

The improved towel clip is designed to facilitate the entrance of the points into the skin. A double curve has been placed in the jaws so that, when the clip is held with the long axis nearly perpendicular to the skin,



FIG. 2.—The slope of the new clip (right) has been reduced to minimize interference.

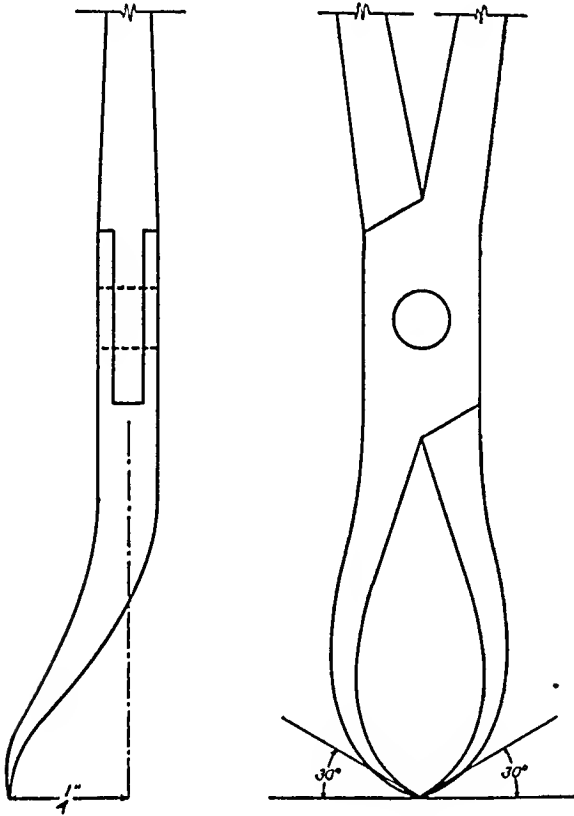


FIG. 3.—Working design of the improved clip.

the points angle down and sink easily into the skin when the clip is closed; but when the clip rests in position on the skin, the points do not angle down into the skin. Figure 1 compares the angle of the tips of an ordinary towel clip and of the improved clip in these two positions. To meet the second defect, the slope of the blades has been reduced so that when the clip is in position on the skin it offers minimum interference. Figure 2 compares the slope of the blades in the ordinary clip and in the improved clip.

Figure 3 gives the dimensions for the manufacture of this type of clip,* which may be obtained in three and one-half- and five and one-half-inch lengths. We prefer the shorter.

The use of this towel clip has permitted accurate and easy fixation of the towel corners to the skin at the line of incision and minimum interference with other instruments.

* This towel clip was made to our designs by Codman and Shurtleff, Inc., Boston, Mass.

BOOK REVIEWS

ATLAS OF OVARIAN TUMORS. By Gemma Barzilai, M.D., with a preface by Fred W. Stewart, M.D. Grune and Stratton, quarto, 261 pages, illustrated with 58 plates, some in color, \$10.00, New York, 1943.

Nothing could furnish better testimony to the enormous interest in the glands of internal secretion in general, and the ovary in particular, than the successive appearance of recent monographs devoted in part or altogether to that organ. In 1940, there was Emil Novak's "Gynecological and Obstetrical Pathology," the best chapters of which concerned tumors of the ovary; in 1942, S. H. Geist's "Ovarian Tumors" appeared, and now, at the beginning of 1943, we have from Dr. Gemma Barzilai an "Atlas of Ovarian Tumors." This handsome monograph has been prepared somewhat in the manner of the magnificent "Atlas du Cancer" brought out in parts during the years 1922 to 1932 by various French pathologists under the auspices of the French Cancer Association and never completed, probably because the depression affected the Rothschild Foundation, which financed it. It consists of a series of reproductions of photomicrographs both in black and white and also in color, with explanatory text conveniently located on the facing page. A useful classification of ovarian neoplasms, with a reasonable histologic and embryologic basis, precedes the text. Most of the names used are conventional and where unusual terms are employed, such as, for example, endosalpingioma, the author gives synonyms in the explanatory text.

The book is addressed particularly to the pathologist who has the difficult assignment of diagnosis by histologic criteria. From this point of view certain weaknesses are apparent. One could not, I believe, from an examination of the illustrations and text, be able to distinguish between theca cell tumor, fibroma and fibrosarcoma. This leads to the general criticism that the detail pictures are not sufficiently magnified to enable one to observe the finer aspects of cellular morphology. Accurate cytologic detail is just as important in the interpretation of ovarian tumors as it is in any other branch of oncology.

The material for the monograph was accumulated in Vienna, Milan, Padua and Istanbul. The text is clearly presented in excellent English, without too many dogmatic statements. It will prove an interesting addition to the library of anyone interested in the subject.

ARTHUR PURDY STOUT, M.D.

OPHTHALMOLOGY AND OTOLARYNGOLOGY—MILITARY SURGICAL MANUALS II. Edited by the National Research Council. W. B. Saunders Company, 331 pp., 188 ills., \$4.00. Philadelphia, 1942.

This manual, as stated in the preface, is not intended to be a complete treatise on ophthalmology or otolaryngology. There are only 303 pages, 157 devoted to ophthalmology and 146 to otolaryngology. It was designed to supply certain specialized information concerning injuries and diseases of the eye, ear, nose and throat that are most likely to occur among troops in time of war, either while in training or during actual combat, and especially to aid the physician when so situated that more detailed special knowledge cannot be obtained. The names of the authors of the various chapters of which this book is composed are guarantees for the reliability of the information recorded in its pages and we have no criticism as to the accuracy of the statements made or the recommendation for the treatment and diagnosis suggested. What is said

is reliable, up to date, and authoritative, and there are some chapters that give data frequently omitted from even the most extensive text book. However, we feel that certain aspects of the book are open to criticism.

First, a multitude of authors have apparently interfered with the coordinated arrangement of the subject material, the book being more like the getting together and binding up of a lot of pamphlets than a teaching manual.

Again, there seems to be a difference of purpose between the part on ophthalmology and on otolaryngology as to the clientele for whom the book is intended. From the preface on ophthalmology we quote, "This compendium is not intended to be a treatise on ophthalmology, nor is it designed for the experienced ophthalmologist." One would infer that it was designed for the general practitioner. Whereas in the preface to the part on otolaryngology again we quote, "No attempt has been made to present elementary principles and practice, as it is fair to assume that commissioned otolaryngologists . . . have been trained beyond any such requirement." Perhaps these two statements help explain the differences in the amount and detail of the subject matter in the different chapters and why the ophthalmologic part is so much more detailed and extensive than the otolaryngological. In otolaryngology there are two chapters spent on the diagnosis and treatment of petrositis, a subject which requires the utmost of specialized training, while there is scarcely a word concerning the method of examining the ear for functional disturbances. Yet in the part on ophthalmology there are two chapters devoted to functional testing and methods of examining the eye..

Also we wonder why some 42 pages are devoted to facial maxillary surgery which the otolaryngologist in civil practice usually turns over to the maxillofacial surgeon. Useful knowledge yes, but this space could have been more appropriately used for more detailed data concerning real otolaryngologic problems even to the inclusion of some subjects that have been omitted on account of lack of space.

However, in spite of these criticisms, we feel that this manual has a distinct place as a quick reference book for the field surgeon with accurate information which for the greater part is concisely and clearly stated. It is well printed, carefully indexed and the illustrations though not profuse are of distinct help in clarifying operative technic.

GEORGE B. WOOD, M.D.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.



LOBECTOMY FOR PULMONARY TUBERCULOSIS

COLONEL EDWARD D. CHURCHILL, M.C., A. U. S.

AND

ROBERT KLOPSTOCK, M.D.

Boston, Mass.

FROM THE HARVARD MEDICAL SCHOOL, AND THE SURGICAL SERVICES OF THE
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

"RESECTION OF LUNG TISSUE is very hazardous in the presence of a positive sputum. If possible collapse therapy is preferred." This is the conclusion drawn from a compilation of the recorded cases of pulmonary resection for tuberculosis by recent authors.³ In as rapidly developing a field as thoracic surgery, impressions drawn from past experience are notoriously misleading. This is particularly true if a reportorial account of experience is taken at its face value, without critical analysis.

The assembled cases of tuberculosis in which pulmonary resection has been carried out form an exceedingly heterogeneous group. Of 80 cases recorded as having been subjected to pneumonectomy or lobectomy, 30 came to operation with an erroneous diagnosis. This can only mean that the preoperative estimate of the situation and, consequently, the time of operation and the technics employed were not in terms of the pathology of tuberculosis. These operations were not performed "for" tuberculosis—the true nature of the disease was discovered too late for the observance of important elementary principles.

Twelve other cases were operated upon after collapse therapy had failed—always an added technical burden. Other cases were resected because of bronchiectasis, intractable hemorrhage, or in the presence of the fever and toxicity of bronchial strictures.

In the lobectomy group no reference to the surgical technics employed is made. Kent and Blades² conclude from their anatomic dissections that the application of individual ligation technic to the right upper lobe is possible, but appear to know of only one instance in which lobectomy has been thus performed. These authors state that as far as the left upper lobe is concerned, "except under unusually favorable circumstances, the individual ligation technic for resection will be hazardous or impossible."

Resections of upper lobes, both right and left, by individual ligation

technics have been routinely performed in this hospital since 1936, and total 21 in number.

While it seems unlikely that the opinions of Kent and Blades reflect a general belief, they at least suggest that a considerable number of the lobectomies for tuberculosis collected by Thornton and Adams³ may have been carried out by the tourniquet technic. This is a procedure eminently successful in bronchiectasis but if applied to a tuberculous lesion would seem predestined to invite empyema, bronchial fistula, or both.

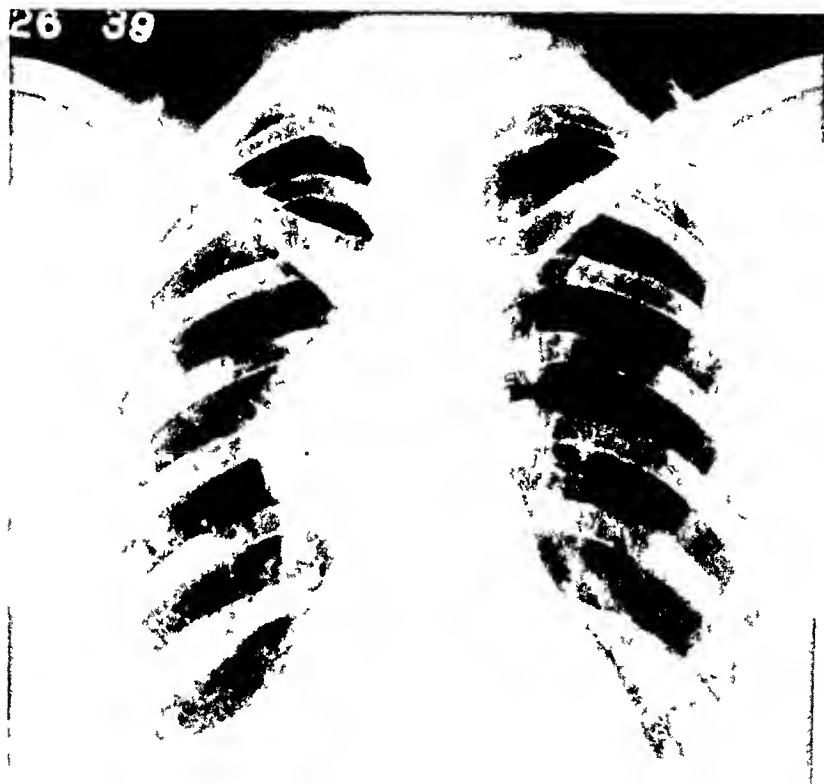


FIG 1a—Preoperative, May, 1939. Oval shadow of increased density in the apex of the right lower lobe. An irregular cavity present in the mass.

Not content to accept a conclusion based on the disasters and prejudices of the past, it seems desirable to present new evidence regarding what may be accomplished at the present time. The cases herewith reported are successive⁴ lobectomies performed for pulmonary tuberculosis. All had positive sputum. All were operated upon with a preoperative diagnosis of tuberculosis.

Discussion of total pneumonectomy in tuberculosis is intentionally omitted, despite a relatively large and favorable personal experience with this pro-

* One other case in which lower lobectomy was performed for bronchial stenosis following upper thoracoplasty has been intentionally omitted, although the patient is alive and well, with complete healing. The case illustrates different surgical principles. Grouping dissimilar cases creates the illusion of impressive numbers, but obscures important principles from which conclusions may be drawn.

LOBECTOMY FOR TUBERCULOSIS

cedure. It is quite another topic. The principles that introduce total pneumonectomy into the treatment of tuberculosis are totally different from those that underlie lobectomy. At the present time, total pneumonectomy cannot be considered an alternative to collapse therapy *provided that collapse*

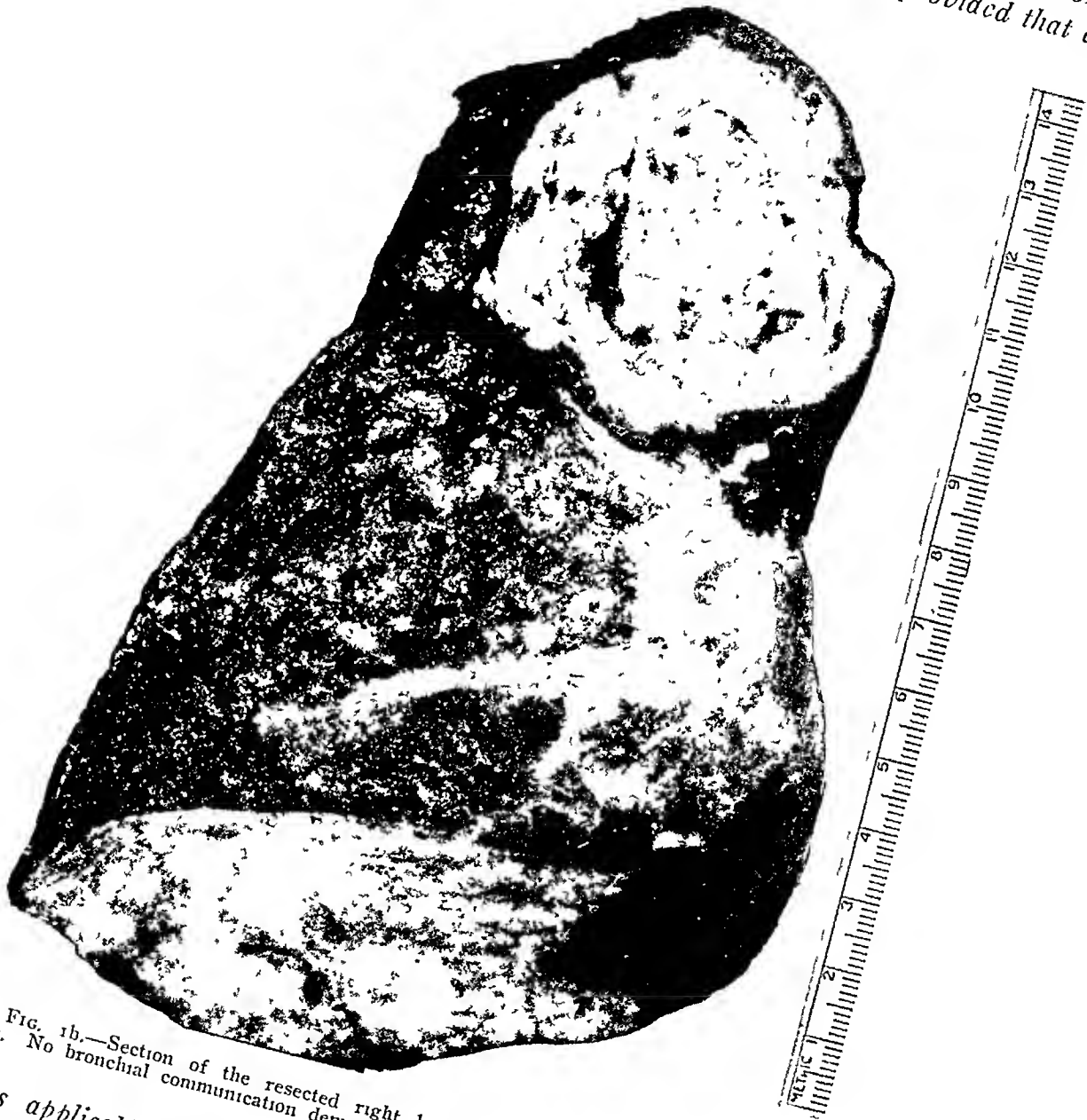


FIG. 1b.—Section of the resected right lower lobe. Well encapsulated caseous mass. No bronchial communication demonstrable.

therapy is applicable to the case under consideration. It is both irreversible and nonselective. It irrevocably and seriously limits any therapeutic procedure that may be needed for the lung of the contralateral side. Circumscribed by strict indications, total pneumonectomy in tuberculosis may be a life-saving operation when no other procedure is feasible.

Lobectomy, on the other hand, is proposed as a *highly selective measure* for dealing with certain unilobar lesions. It is, indeed, far more conservative

of pulmonary function than even a seven rib thoracoplasty. Whether or no it is more selective than a skilfully controlled artificial pneumothorax is open to debate. Properly used, artificial pneumothorax has the advantage of being a reversible form of therapy. The therapeutic goal is a re-expanded healed lung. As lobectomy is by definition irreversible, it can be suggested as an alternate to artificial pneumothorax only when tuber-

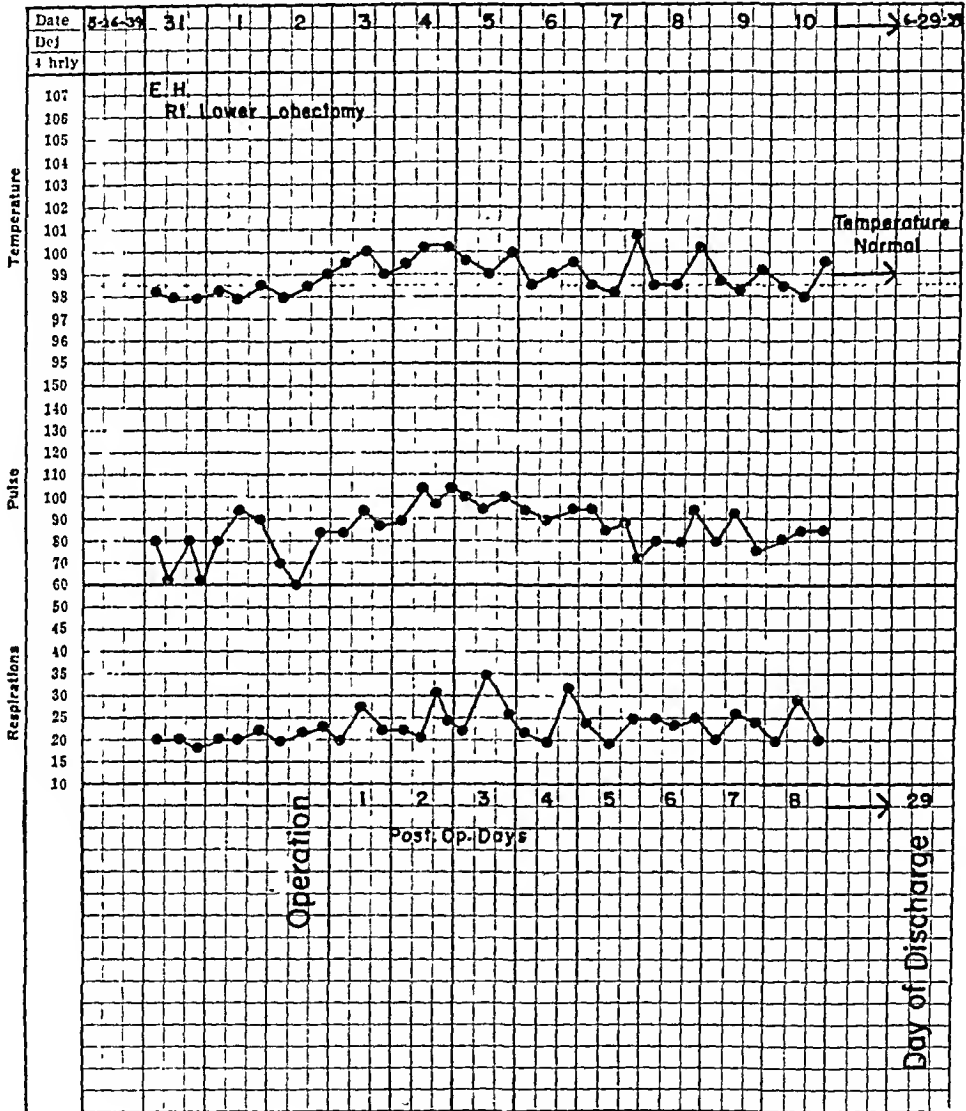


FIG. 1c.—Postoperative chart.

culosis has produced *irreversible* or *irreparable* destruction of lung substance. In these instances the strategy of a temporary reversible measure such as artificial pneumothorax is lost in the dilemma of either maintaining the collapse indefinitely, or facing reactivation by withdrawal.

The first three case records stand as instances of indications for lobectomy that can hardly be challenged as a departure from accepted surgical and

LOBECTOMY FOR TUBERCULOSIS

pathologic reasoning. Cases 4, 5 and 6, however, carry the matter further. Here, orthodox indications for thoracoplasty were disregarded, and a deliberate election of lobectomy substituted. Operation having been successful, it must be granted that *in these individual patients* lobectomy was preferable to thoracoplasty. The only question remaining is how frequently can such satisfactory results be achieved in a series large enough to be statistically significant. This can only be answered by further experience.

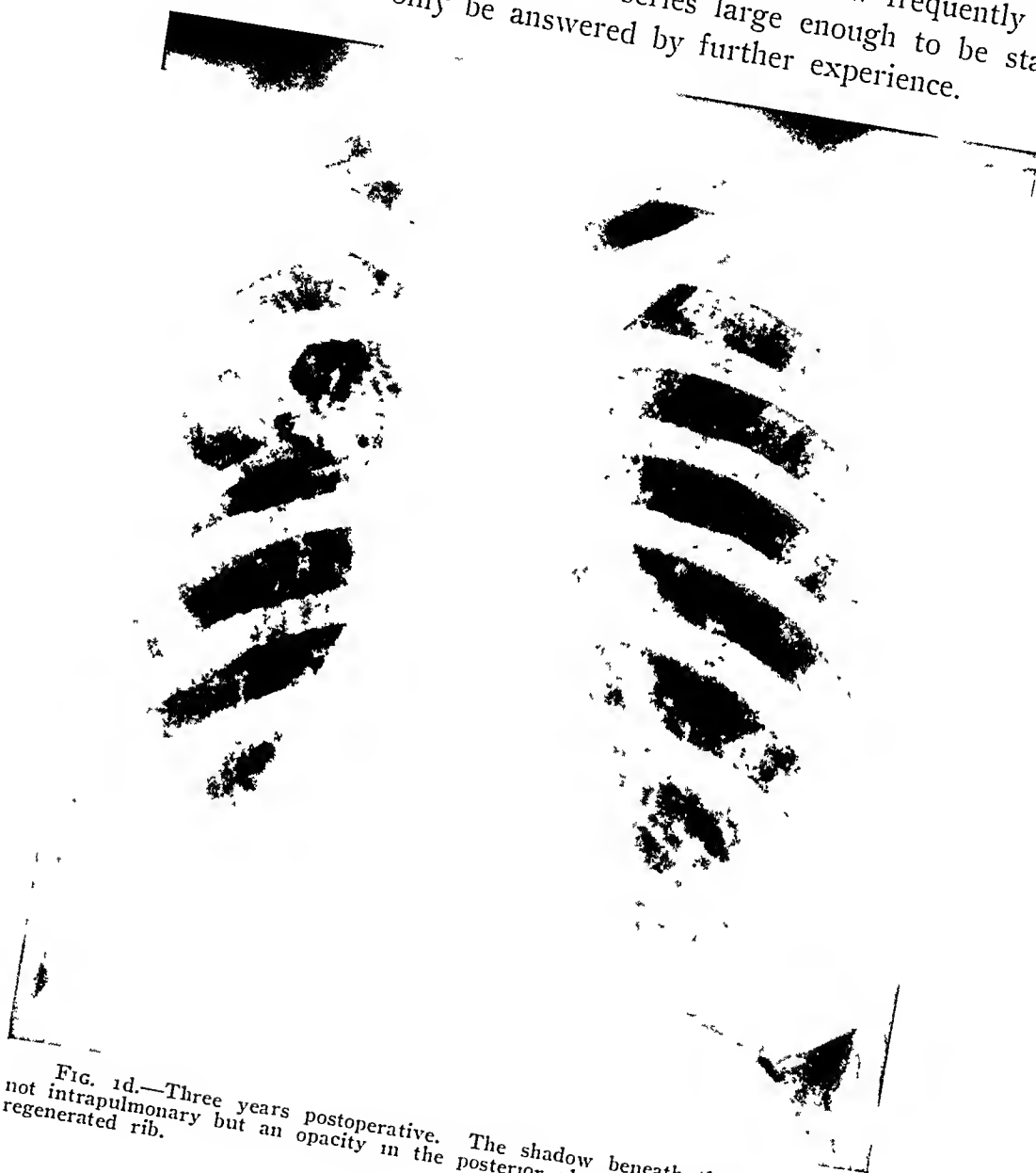


FIG. 1d.—Three years postoperative. The shadow beneath the 5th rib is not intrapulmonary but an opacity in the posterior pleura, continuous with the regenerated rib.

CASE REPORTS

Case 1.—U No. 194756: E. H., female, age 38 when she entered the Massachusetts General Hospital in May, 1939. She reported a run-down condition of 10 to 15 years' duration with increased susceptibility to respiratory infections. A "cold" in January, 1938, left a persistent cough. Roentgenograms and physical examination of the chest revealed an infiltration in the apex of the right lower lobe. *Sputum was positive for tuberculosis* in March, 1938. She entered a Saranac Lake sanatorium, where the sputum became "negative" in August, 1938, and remained so. The recovery seemed very satisfactory, although the area of density in the right hilum gradually increased

in size and showed a cavity in the center. Bronchoscopy and the bronchogram were uninformative. Several physicians considered that the appearance of the lesion was atypical for tuberculosis. Both malignancy and chronic lung abscess were considered.

On entry to this hospital the patient was essentially free of symptoms, her sputum was minimal in amount, and negative. The roentgenologist described an oval mass in the apex of the right lower lobe in contact with 6th and 7th dorsal vertebrae, measuring 6.5 x 4.5 cm. in diameter. An irregular cavity, with possible fluid level, was present in the mass. The periphery of the mass was smooth. There was definite thickening of the pleura overlying the vertebrae. The left lung was clear. The findings were considered consistent with tuberculosis, although admittedly unusual (Fig. 1a).

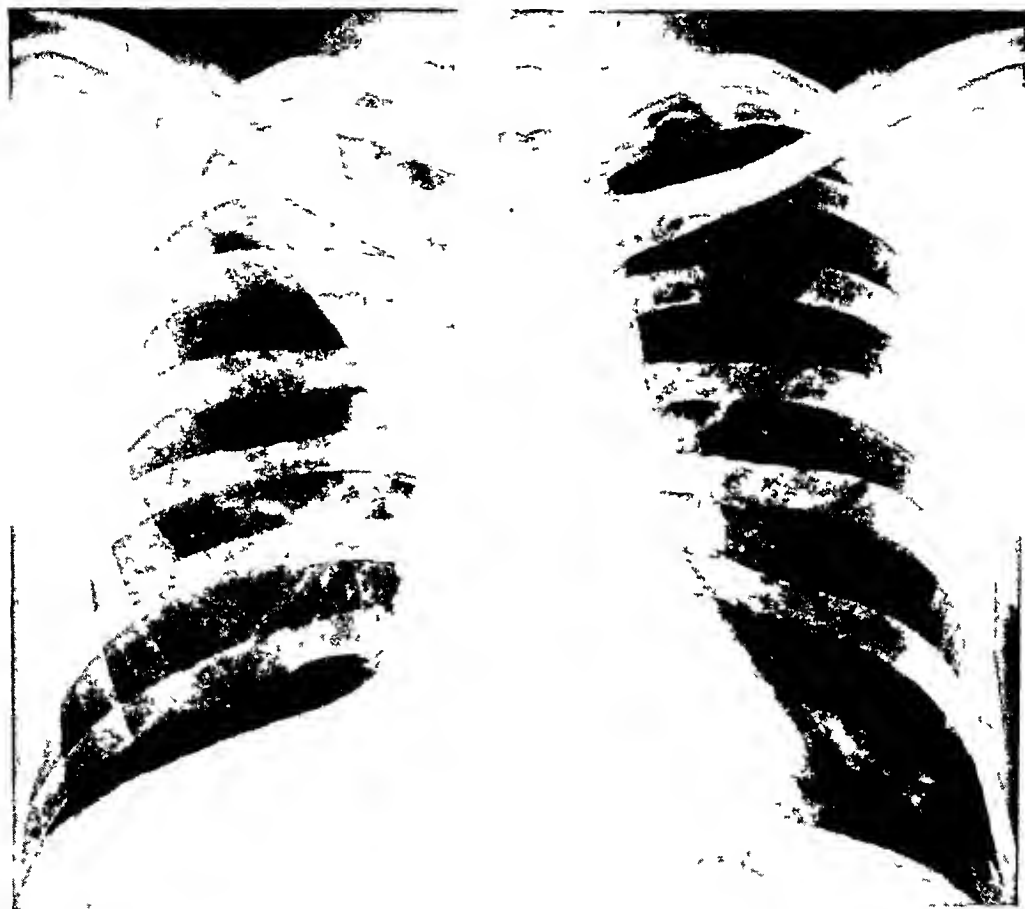


FIG 2a—Preoperative, November, 1941. Partially collapsed right upper lobe.

Operation.—6-2-39: Resection of the right lower lobe, with individual ligation technic.

Pathologic Examination.—In the apex of the right lower lobe was a caseous mass, well encapsulated, containing an irregular cavity (Fig. 1b). No free bronchial communication. A few scattered foci, pleural and subpleural, were present. *Smear from caseous material was loaded with acid-fast bacilli.*

Postoperative Course.—Uneventful. Patient was discharged on the 29th post-operative day in good health (Fig. 1c). She has been well since.

Postoperative Roentgenologic Examination.—June, 1942, three years after operation, negative for tuberculosis. Pleural scar in region of the 2nd rib (Fig. 1d).

COMMENT: This case represents the well known problem of the hilar round shadow, with or without cavitation. The majority of these are

LOBECTOMY FOR TUBERCULOSIS

found in the apex of the lower lobe. The "hilar" tuberculous lesion is the stepchild of surgical collapse therapy; disappointing results are likely to be obtained with any or all forms of treatment. Single foci in this location are usually hematogenous in origin without further tuberculous changes in the lung except for discrete, subpleural seeding in the same lobe. The latter

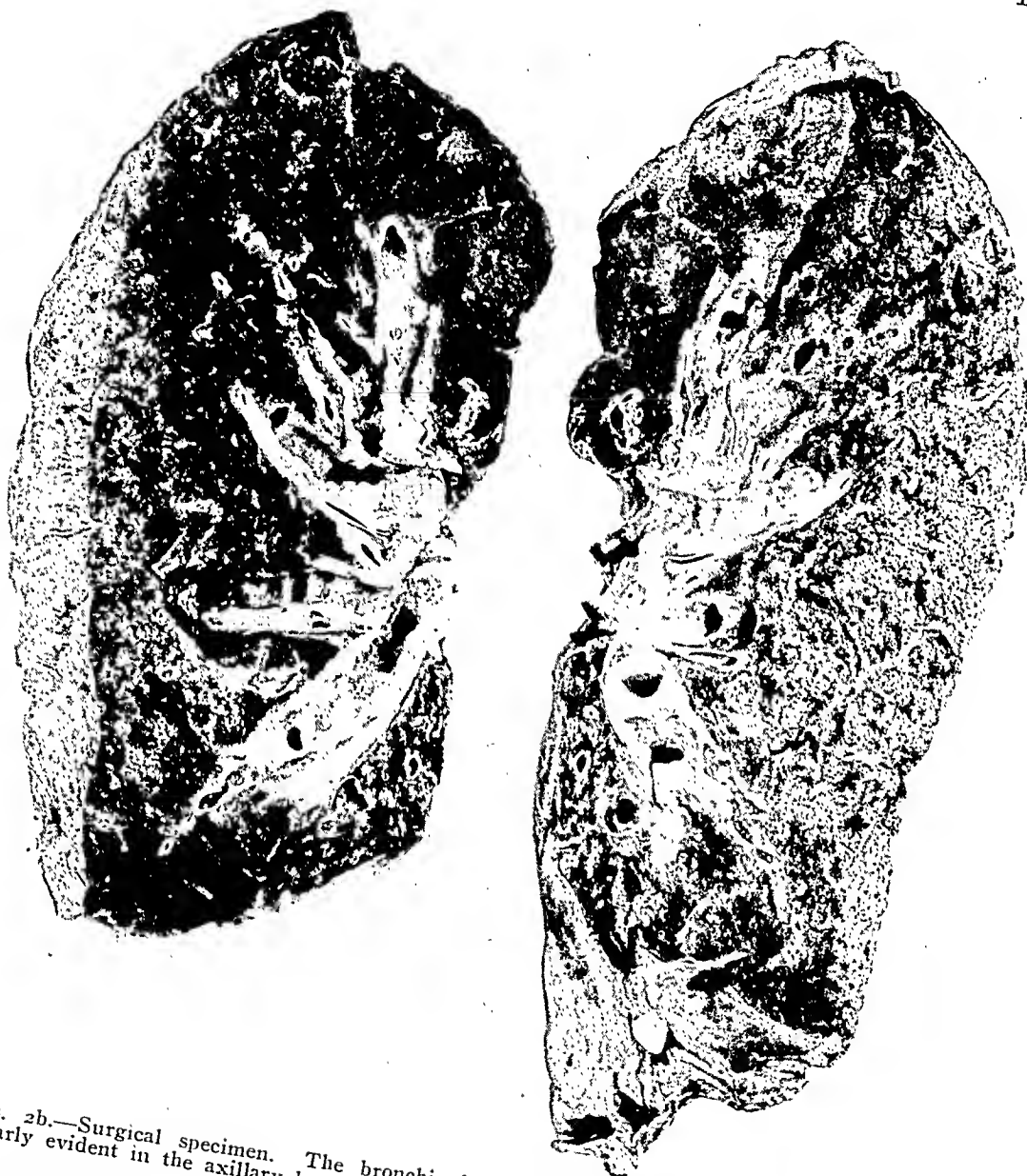
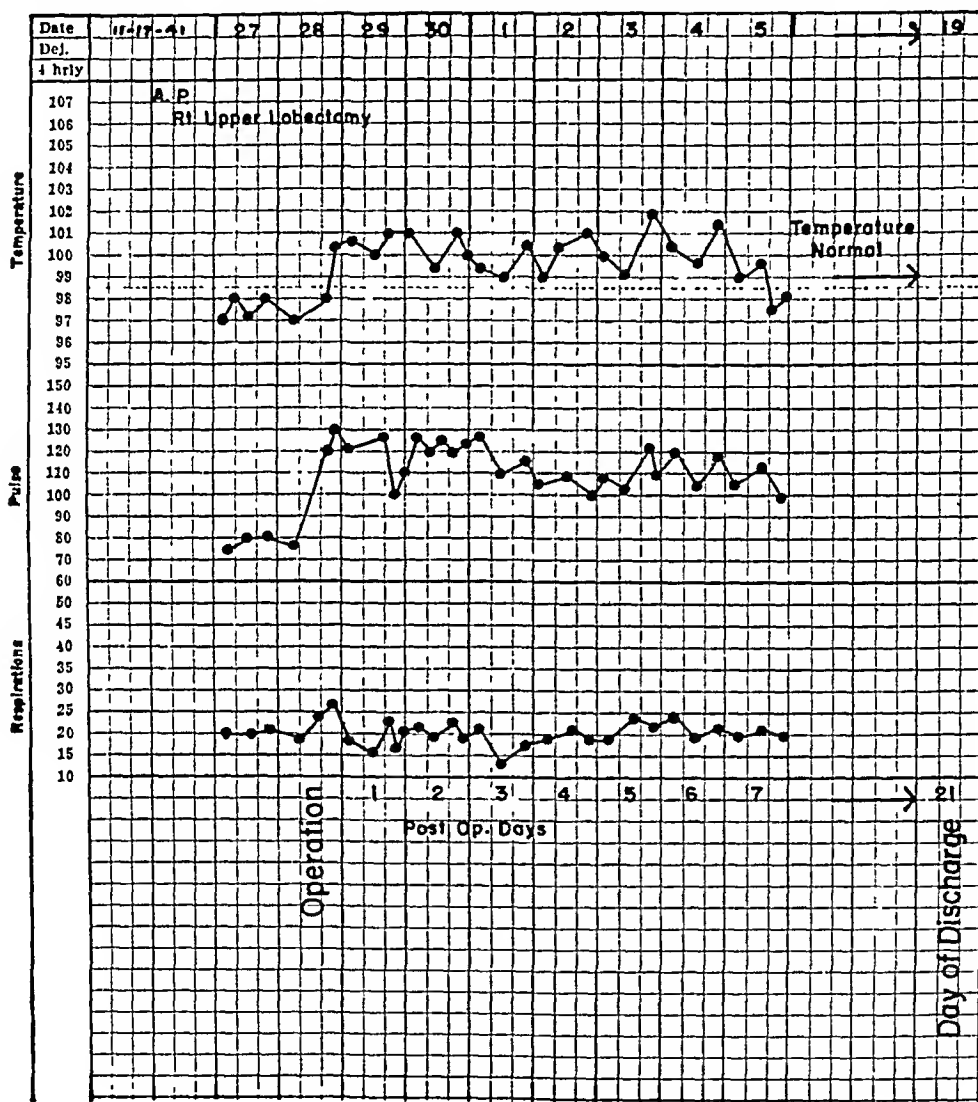


FIG. 2b.—Surgical specimen. The bronchi show a coarsely granular mucosal surface, particularly evident in the axillary branch. Microscopic changes throughout.

is a characteristic part of the pathologic pattern designated as "hematogenous." Massive foci are either the rather common "early round infiltration" with liquefaction that progresses slowly, or the so-called "punched-out" cavities, which are likely to be blocked and converted into a single caseous round focus. They closely resemble tumors, and are occasionally mistaken for lung abscesses. The findings in the present case are consistent with an early round infiltration in the state of protracted liquefaction.

Case 2.—U No. 329952: A. P., male, age 38, was admitted to the Massachusetts General Hospital in November, 1941. His previous history revealed that one and one-half years before entry, on a routine roentgenologic examination, a dense and contracted right upper lobe was found. Both sputum and gastric contents were *positive* for tuberculosis. At the Sanatorium of the Metropolitan Life Insurance Co., the patient was treated by bed-rest. A bronchoscopy revealed obstruction of the right upper lobe bronchus by a lesion described as a tuberculous granuloma. The condition of the patient remained satisfactory but the roentgenologic findings did not change. The minimal



LOBECTOMY FOR TUBERCULOSIS *

Pathologic Examination.—*Gross:* A partially collapsed, anthracotic upper lobe, the pleural surface of which was smooth except for two small bands at the apex. Two major bronchi showed a coarsely granular mucosal surface, one a healed granuloma. There was no macroscopic parenchymal tuberculous lesion of any appreciable size. Those present were consistent with caseous bronchitis of the smaller and smallest bronchi. Scattered, grayish, small foci of fibrosis, some emphysema, numerous slightly dilated bronchi (Fig. 2b). *Microscopically,* studies revealed an almost uniform tuberculous pattern (Fig. 2b). *Postoperative Course.*—Uneventful. The patient was discharged on the 21st post-operative day (Fig. 2c).

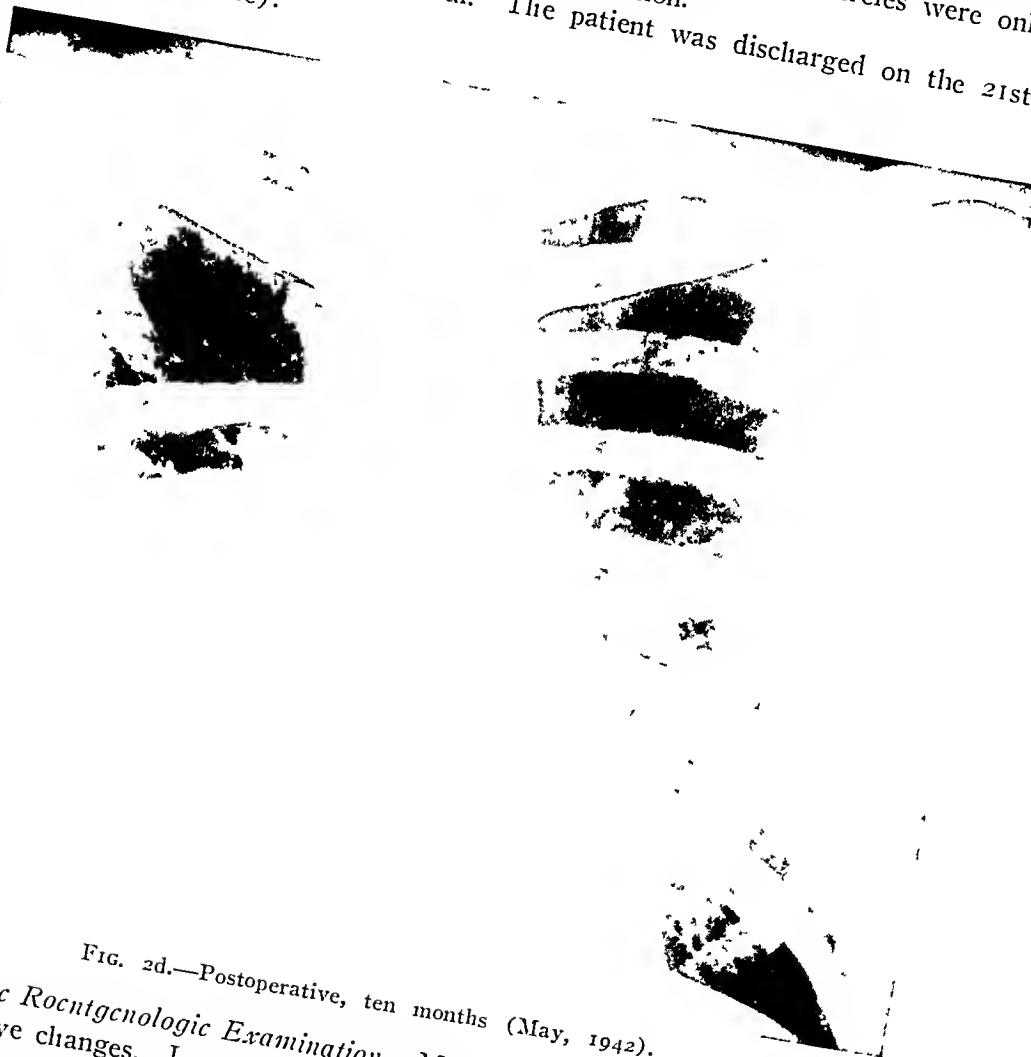


FIG. 2d.—Postoperative, ten months (May, 1942).

Postoperative Roentgenologic Examination.—May, 1942: Shows no pathology beyond usual postoperative changes. Lower lobe completely reexpanded. The elevation of the diaphragm is due to crushing of the phrenic nerve (Fig. 2d).

Case 3.—U No. 360821: H. P., female, age 32, mother of one child, entered the Massachusetts General Hospital from the Rutland State Sanatorium in June, 1942. The patient had been well until May, 1941, when she developed a "cold" which persisted as a severe chronic cough. She was fluoroscoped in June and a "bronchial trouble" diagnosed. In July, 1941, she was admitted to a Worcester, Massachusetts Hospital because of severe cough accompanied by fever of 103° F. There she was treated for pneumonia, according to the patient's report. After discharge from that hospital she went to a physician who found tubercle bacilli in her sputum. She was referred to the Rutland State Sanatorium and admitted there. On admission the chest film revealed a process in the right upper lobe, which appeared decreased in size. In

the basal third of the right upper lobe was an homogeneous density with sharp marginal demarcation towards the lower and middle lobe (Fig. 3a). The findings were considered consistent with tuberculous infiltration, although collapse was recognized as a part of the pathology. The suspected tuberculous involvement of the right upper lobe bronchus could not be confirmed at that time. Artificial pneumothorax on the right side was instituted and maintained (Fig. 3b). The patient's symptomatic recovery was good, she gained twenty pounds, but her sputum continued to contain tubercle bacilli.

Operation.—7-9-42: The right 4th rib was resected and the right chest was opened. The lung was found collapsed due to the previous pneumothorax. When positive



FIG. 3a.—On admission to the Rutland State Sanatorium, 1941. Right upper lobe decreased in size exhibiting an homogeneous density in the basal third.

pressure was applied the two lower lobes, *i.e.*, the middle and lower lobes, they expanded well but it was impossible to demonstrate any aeration of the upper lobe. A clamp was placed on the visceral pleura of the upper lobe to be used for traction purposes, and, from above downward, the lobe was dissected free from mediastinum and azygos vein where it was densely adherent. The structures at the hilum were isolated singly and the vessels doubly ligated. The lobe was then freed from the middle lobe. The ascending artery was identified and doubly ligated. The bronchus to the upper lobe was found to be partially stenosed by scar. The bronchus was closed. Denuded areas, particu-

LOBECTOMY FOR TUBERCULOSIS

larly over the azygos vein, were covered with pleura and the wound closed without drainage after the middle and lower lobes were expanded. Only a small amount of blood was lost during the entire procedure.

Pathologic Examination.—*Gross:* A Completely consolidated small right upper lobe. Upon section, the bronchi appear dilated and some of them coated with a thin caseous layer; others appear to be obliterated. In a small area there was a localized miliary caseation. This excavation could be seen. *Microscopically,* the histologic appearance of the tuberculous lesions was exactly similar in character to that of the preceding case, although this lobe showed more extensive pathology. The lesions

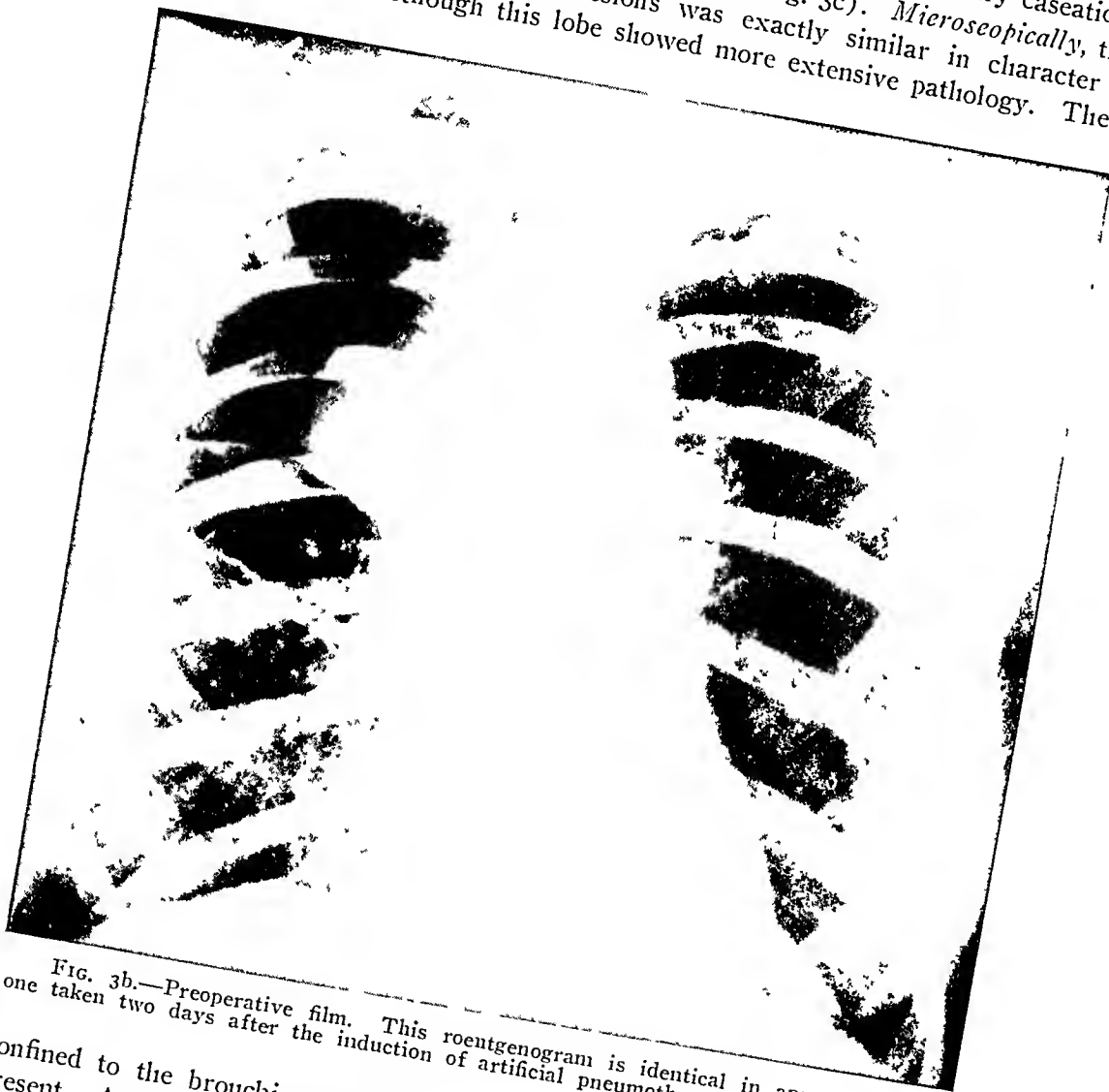


Fig. 3b.—Preoperative film. This roentgenogram is identical in appearance with one taken two days after the induction of artificial pneumothorax.

were confined to the bronchi and bronchioles. Large areas of fibrosis and atelectasis were present. At the base, posteriorly, a recrudescent Ghon focus could be seen. The hilum in the region of dissection was free of tuberculous nodes. The peribronchial lymph nodes contained small caseous foci.

Postoperative Course.—Uneventful. The patient was discharged on the 22nd day (Fig. 3d).

Postoperative Roentgenologic Examination.—Shows the condition August 3, 1942, four weeks after operation. Some apical fluid or apical thickening of the pleura is still present (Fig. 3e) although the Rutland State Sanatorium reported good breath sounds all over the chest at that time. On February 1, 1943, she is reported to be in perfect health, with fluoroscopic findings normal except for paralysis of the right diaphragm.

COMMENT: Cases 2 and 3 exhibit the peculiar pathologic pattern of unilobar tuberculous involvement of the bronchi, large and small. As to pathogenesis, an hematogenous origin is the most probable. Aspiration as the cause of this caseous bronchitis appears out of question, since there is no liquefying focus or chronic cavity to provide so thorough a seeding. Unilobar caseous bronchitis is likely to be erroneously considered as an infiltrative or exudative lesion due to the dense homogeneous roentgenologic appearance and sharp marginal demarcation. The third case (H.P.) demonstrates better than any statement the effect of collapse therapy upon a lobe the bronchi of which are diseased. The induction of the pneumothorax was followed by an immediate and complete collapse, giving in two days an appearance identical



FIG. 3c.—Surgical specimen. Cut surface of the resected lobe. See the note on the pathology of this specimen.

to the film reproduced in Figure 3b. Such an occurrence in the early phase of pneumothorax therapy should be regarded as an indication that one is not dealing with an infiltrative process which can be successfully treated by collapse therapy. This type of underlying pathology leads to the complication of the unexpandable lung. Even the most ideal and long standing collapse may not lead to healing of the tuberculous process if there has been an incorrect interpretation of the pathology. Thoracoplasty would have been equally ineffective. Ablation of the involved lobe seems the only feasible form of therapy.

Case 4.—U No. 345056: L. F., female, age 22, was admitted in March, 1942, from the Rutland State Sanatorium. Her disease was discovered in October, 1941, by a routine roentgenologic examination following a diagnosis of pulmonary tuberculosis made on her brother one month earlier. She was found to have an indurative tuberculosis, with cavitation in the right upper lobe, and positive sputum. She was admitted immediately to the Rutland State Sanatorium. Therapeutic pneumothorax could not be established because of obliteration of the pleural space, therefore, she was kept on bed-

LOBECTOMY FOR TUBERCULOSIS

rest for six months. On admission to the Massachusetts General Hospital the patient was in excellent condition. A roentgenogram showed mottled dullness in the right first interspace and the right apex. Within the mottling in the first interspace there was a cavity 2.5 cm. in diameter, lying in the posterolateral aspect of the lobe. This film showed essentially the same condition that had existed on admission to the Rutland State Sanatorium- (Fig. 4a).

Operation.—4-27-42: Right upper lobectomy. Adherent and obliterated pleural space

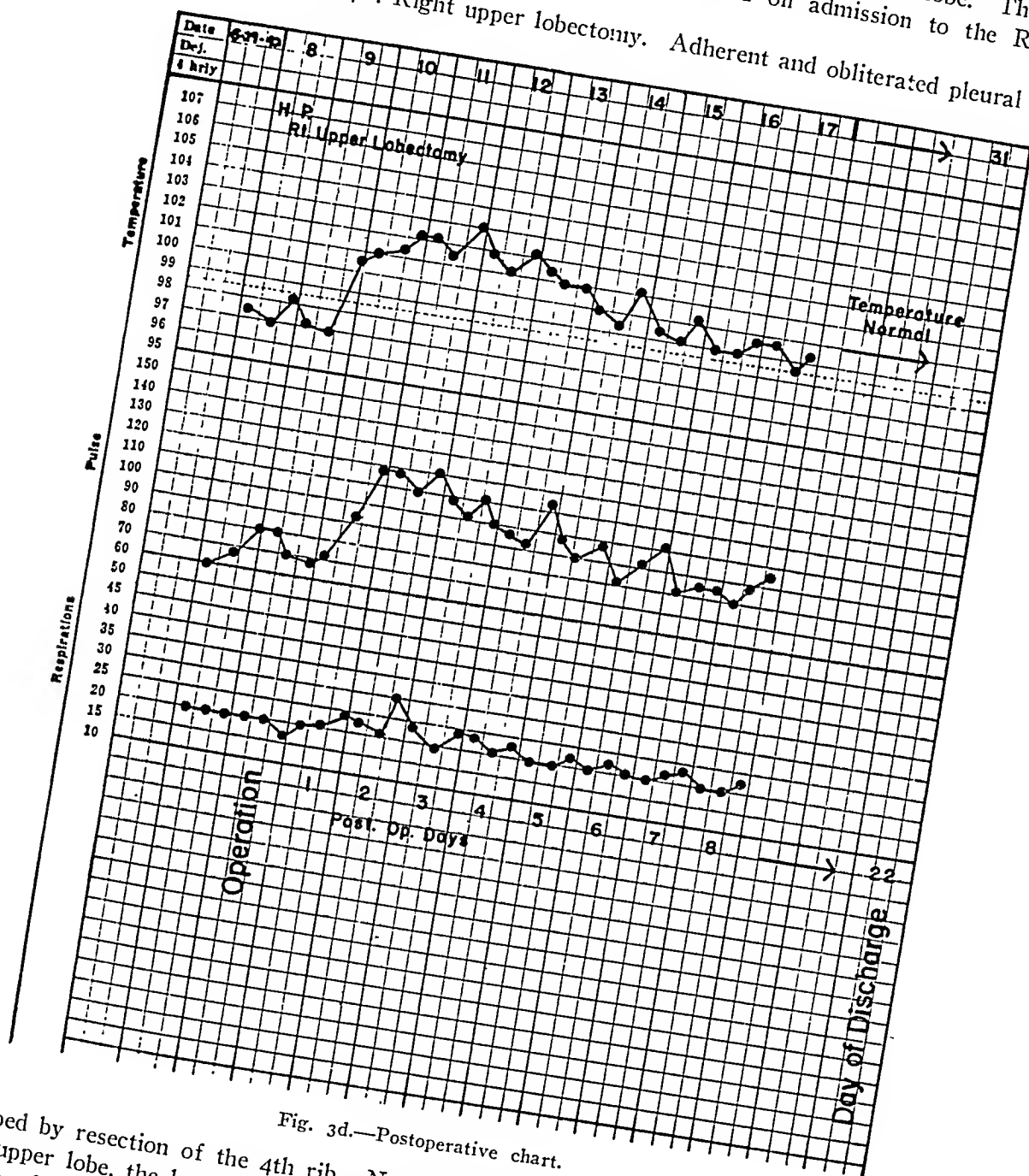


Fig. 3d.—Postoperative chart.

developed by resection of the 4th rib. Near the angle of the ribs in the lower portion of the upper lobe, the lung was densely adherent to the parietal pleura over the cavity. A patch of parietal pleura, approximately 3 cm. square, was excised to keep the plane of mobilization at a distance from the wall of the cavity. The remainder of the parietal surface of the lobe was easily mobilized, although everywhere adherent. Considerable care was necessary in dividing the fissures, the one with the lower lobe being involved in the inflammatory reaction of the disease, and the anterior portion of the middle lobe fissure being anatomically very incomplete.

After these were developed the hilum was easy to dissect, ligating the superior branch of the pulmonary artery in two divisions and the superior pulmonary vein in three branches. No ascending upper lobe artery was identified. It was believed to be absent. The bronchus was isolated and secured with a catgut mattress suture. It was amputated at its first division and the end closed with interrupted silk after cauterizing the mucous membrane with phenol. No pedicle flap was available for coverage. The mediastinal pleura was sutured over it and, after crushing the phrenic nerve at the level of the azygos vein, the hilar portion of the lower and middle lobes could be drawn up to cover the bronchial stump.

The adhesions of the dorsal segment of the lower lobe to the parietal pleura were divided to allow its ascent toward the apex. The lower part of the pleural cavity was



FIG. 3c.—Roentgenogram of the chest four weeks after operation (August 3, 1942). No tuberculous pathology visible.

found completely obliterated. The pleural space was dusted with four grams of sulfanilamide, and the incision closed with silk, without drainage. Air was aspirated.

Pathologic Examination.—*Gross:* The specimen shows the posterior part of the right apex changed by radiating induration of rubber-like consistency. At the center lies a "punched out" cavity the inner surface of which is coated with a very thin caseous exudate. A small bronchus, the only one, leading toward the cavity is obliterated. The superior and anterior part of the apex exhibits an irregular gray scar intermixed with emphysematous parenchyma representing a healed lesion of earlier date (Fig. 4b).

Postoperative Course.—This was, as in preceding cases, extremely smooth and uneventful. She was discharged on the 35th postoperative day (Fig. 4c). One month after operation tuberculin tests (1:50,000 and 1:20,000 O.T.) were negative. She is living with her family at home.

LOBECTOMY FOR TUBERCULOSIS

Postoperative Roentgenologic Examination.—July, 1942: Showed no pathology except usual postoperative changes (Fig. 4d).

COMMENT: This patient was deliberately chosen, with her consent, for lobectomy as preferable to a thoracoplasty. Artificial pneumothorax was impossible.

CASE 5.—U No. 373702: E. S., female, age 22, was admitted to the Massachusetts General Hospital in September, 1942, from the Channing Home. She had entered the Channing Home in August, 1941, with a history of fatigue and cough of six months' duration. A roentgenogram of her chest at that time showed a cirrhotic process with large multiple cavitations in the right upper lobe and two small liquefied aspiration

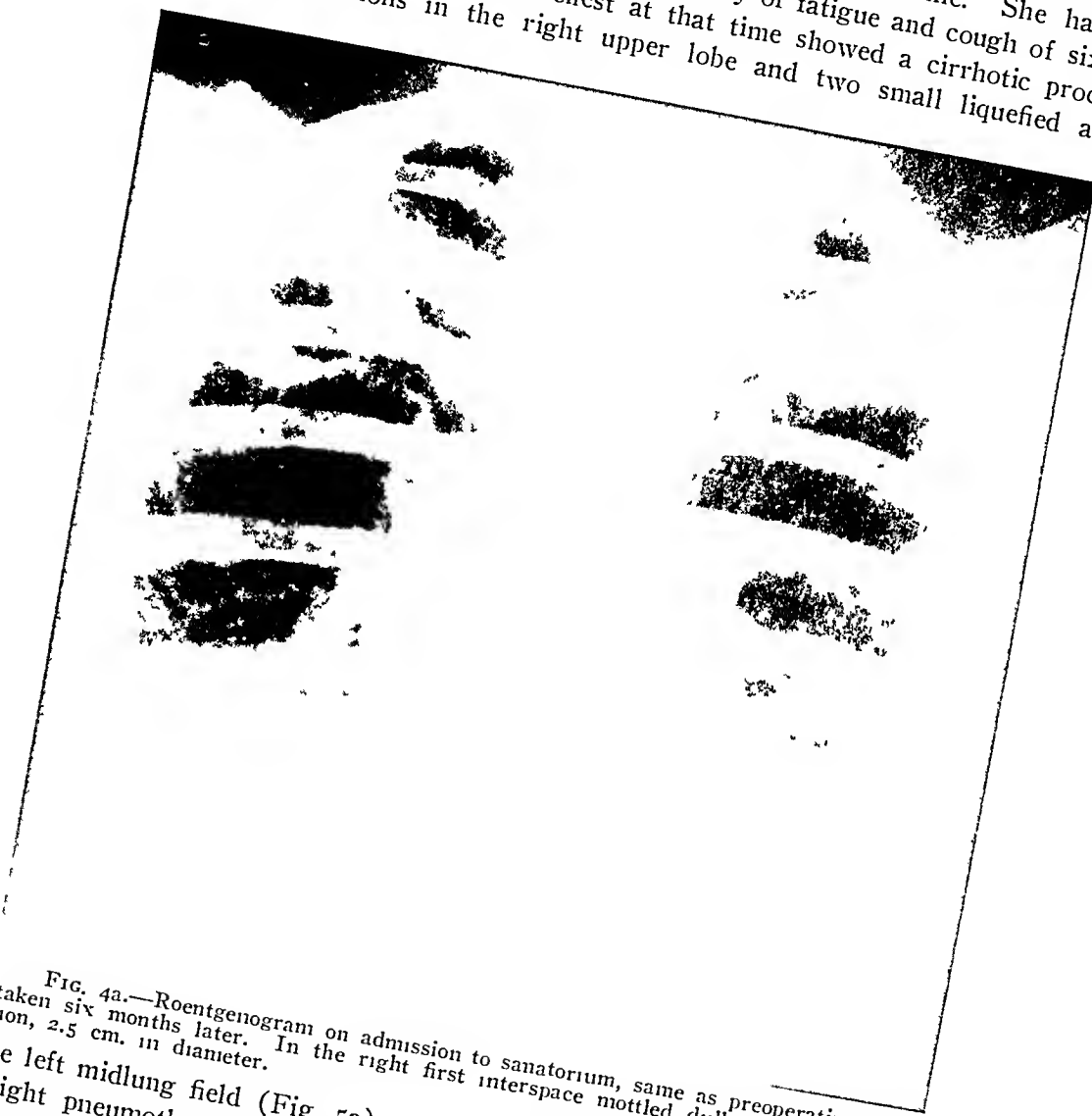


FIG. 4a.—Roentgenogram on admission to sanatorium, same as preoperative film, taken six months later. In the right first interspace mottled dullness with cavitation, 2.5 cm. in diameter.

foci in the left midlung field (Fig. 5a). Sputum was strongly positive. In September, 1941, a right pneumothorax was instituted but was abandoned shortly thereafter because of numerous adhesions. In December, 1941, a pneumothorax on the left side was started but discontinued because of gastric distress. In January, 1942, a right temporary phrenic paralysis was induced. She continued to improve in the Channing Home but in April, 1942, she had a small hemoptysis. Temperature reached a maximum of 99.4° F. The sputum remained strongly positive. On admission to the Massachusetts General Hospital for surgery her general condition was good. A roentgenogram showed essentially the same process as at entry to the Channing Home. The right upper lobe was, in its larger portion, destroyed by cavitation. The remaining parenchyma of the lobe appeared dense.

The left lung was apparently stable but there was a suggestion of a one cm. cavity with some infiltration around it in the mid-lung field, where the cavitation had been demonstrated previously (Fig. 5b). The sputum was loaded with tubercle bacilli. Bronchoscopy was uninformative.

Operation: A right upper lobectomy was performed on September 16, 1942. Under intratracheal gas-oxygen-ether anesthesia, with the patient lying on her left side, the right chest was prepared with iodine and an incision made over the 5th rib. The muscles were divided down to the chest wall. Subperiosteal resection of the 5th rib was done. The pleural cavity was opened through an area free of adhesions, and it was then seen that the right upper lobe was densely bound down by adhesions. An



FIG. 4b.—Surgical specimen. The photograph shows only the diseased area. Note the sclerotic tissue surrounding the cavity.

intrapleural dissection was started and continued until it was found that bleeding was excessive in this plane. Extrapleural dissection was then attempted and found to be more feasible. By combined intra- and extrapleural dissection the upper lobe was entirely freed, bleeding vessels being controlled with dura clips and silk ligatures. The fissure between the middle and lower lobes of the lung was found to be free of adhesions. Following the individual ligation of the pulmonary veins and arteries, the bronchus was isolated, closed with a mattress suture, and cut across. Several sutures were placed to close the bronchus. During the entire procedure there was no contamination of the pleural space nor was the lung tissue opened. The middle lobe was freed so that the end of it could be sutured over the closed bronchus. Four grams of sulfanilamide were dusted into the pleural cavity after hemostasis was complete. The lower lobe was

LOBECTOMY FOR TUBERCULOSIS

entirely mobilized to make expansion of that portion of the lung more complete post-operatively. The chest was closed in layers with multiple interrupted silk sutures. The skin was closed with silk. No drainage.

Pathologic Examination.—A small sclerotic right upper lobe. It is almost completely excavated presenting a large cavity over an area 6 x 8 cm. The excavation extends immediately beneath the pleura and presents a rigid wall surrounded by firm

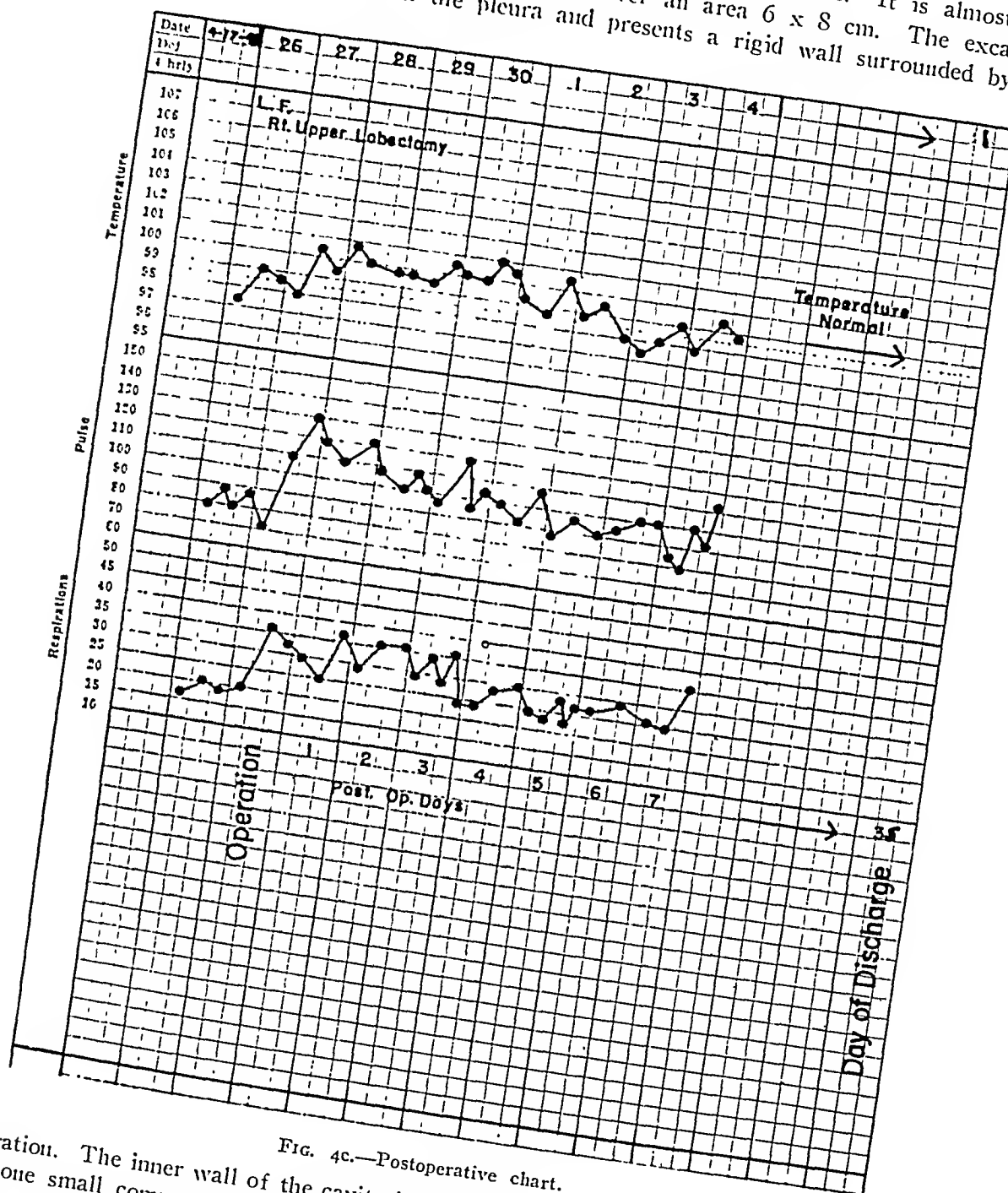


FIG. 4c.—Postoperative chart.

induration. The inner wall of the cavity is coated by a heavy caseous lining and affords only one small communication with the bronchial tree. The rest of the lobe is completely airless and does not show active tuberculous foci. At the very apex there is a layer of fibrous tissue representing extrapleural surgical resection (Fig. 5c).

Postoperative Course.—Uneventful. Patient had no cough and no expectoration whatsoever. Discharged on the 23rd day (Fig. 5d). Preoperative and postoperative tuberculin skin tests showed a sensitivity 1:50,000.

Postoperative Roentgenologic Examination.—December 11, 1942: Showed on the

right side no pathology, other than postoperative changes. The lesion on the left was resolved except for a 1.5 cm. thin wall ring shadow (Fig. 5e). Since the main lesion had been eradicated, the control of the contralateral cavity by pneumothorax became a hopeful therapeutic measure. Accordingly, on December 16, 1942, left pneumothorax was re-established and has been continued (Fig. 5f). In March, 1943, sputum was still positive, and bronchoscopic examination showed no evidence of ulceration or tuberculous granulation in any of the bronchi.

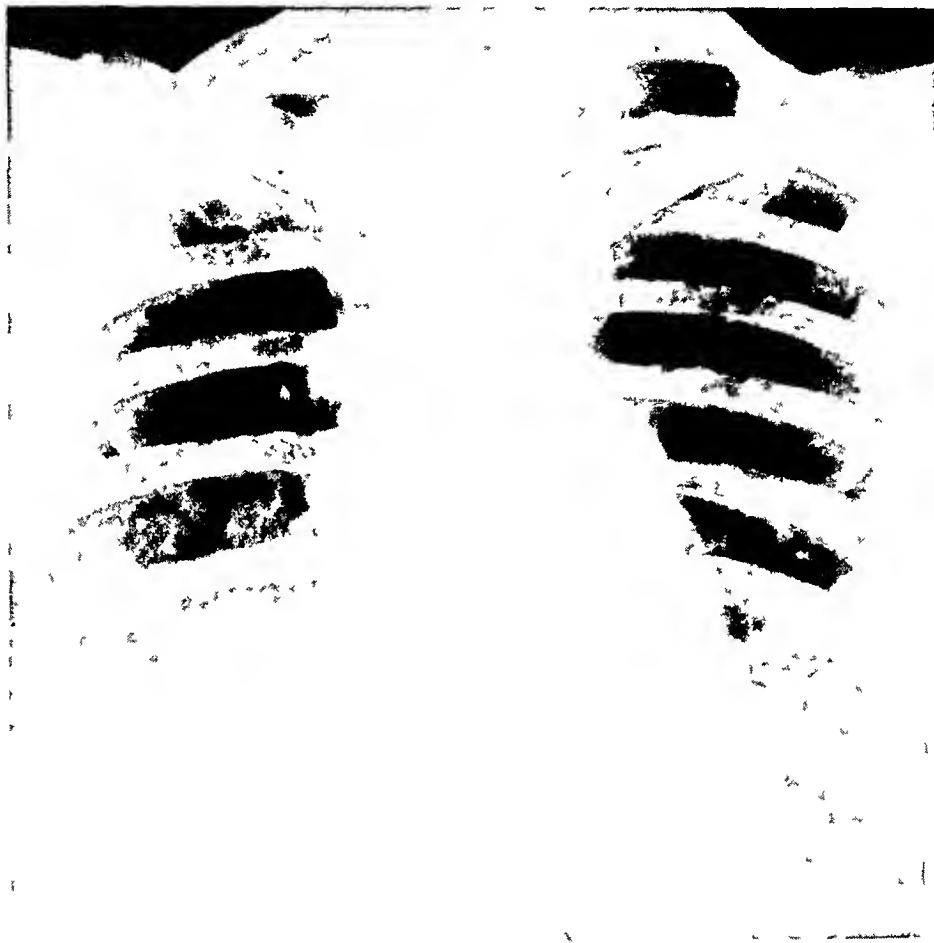


FIG. 4d—Postoperative three months (July, 1942). No tuberculous pathology visible

COMMENT: The case presents the rather crucial problem of contralateral disease in the presence of a giant upper lobe cavity in a young woman, age 24. The contralateral side had exhibited susceptibility to bronchogenic spread and contained two small cavities. Pneumothorax had proved to be ineffective. In accord with usual practice, thoracoplasty would be the method of treatment. Considering the extent of the disease, several stages would have been required to close this cavity and the tiny bronchial communication may well have produced the "block" phenomenon. During the entire course of the surgical program the dangers of bronchogenic aspiration spread would have persisted.

The selective nature of lobectomy is well illustrated in that the chief focus of the disease was eliminated by a single operative procedure that

LOBECTOMY FOR TUBERCULOSIS

FIG. 5a.



FIG. 5b.

FIG. 5a.—August, 1941. Cirrhotic tuberculosis, with extensive cavitation in the right upper lobe. Left midlung field shows two cavities, representing liquefied aspiration foci.

FIG. 5b.—On admission to the Massachusetts General Hospital. The cavities in the right upper lobe enlarged. Lesion on the left side unchanged but obscured by perifocal infiltration.

left the right lower and middle lobes intact. It was then possible to institute a contralateral artificial pneumothorax for the preexisting bronchogenic spread.

Case 6.—U No 377199. M M, female, age 35, was admitted in October, 1942, to the Massachusetts General Hospital. Her first breakdown was 13 years previously—treated with bed rest for two years. Sputum was negative at that time. In 1936, tuberculosis flared up in the left upper lobe. According to the available roentgenogram (Fig. 6a) she had a productive tuberculosis in the left upper lobe with a few circumscribed foci but without visible cavitation.



FIG 5c.—Surgical specimen. Note the size of the cavities, their sclerotic walls and the lack of bronchial drainage with the exception of a single "pin head" size communication with the bronchial tree. There was no reason to predict that a "blocked" cavity existed.

scribed foci but without visible cavitation. The sputum became positive at that time. She was treated with artificial pneumothorax on the left side (Fig. 6b). The treatment was continued for three and one-half years. After reexpansion she was able to lead a normal and active life. In June, 1942, she developed a productive cough. The sputum became *positive* for tubercle bacilli. In July, 1942, she was concerned with marital worries and difficulties and lost 14 pounds of weight. A roentgenogram, however, did not show any change as compared with the one taken after her pneumothorax was discontinued. At that time she also complained of fatigue. She was readmitted to the Channing Home where the pneumothorax had been originally started. The staff of this institution referred the patient for surgery.

On admission to the Massachusetts General Hospital the patient was in good general

condition. The sputum was minimal but contained tubercle bacilli. A roentgenogram (Fig. 6c) showed a shrunken and dense upper lobe on the left side, with scattered, circumscribed foci, varying in size from 2 to 5 mm. in diameter. No cavity was visible.

Operation.—10-14-42: A left upper lobectomy was performed. With the patient under intratracheal gas-oxygen-ether anesthesia, and on her right side, the left chest was prepared with iodine. An incision was made over the course of the 5th rib and curved in order to free the tip of the scapula. The trapezius was divided posteriorly, then the rhomboids and serratus posticus identified. This was separated from its attachment to the 5th rib and subperiosteal resection of the rib carried out. The pleural cavity was entered. Dissection of the left upper lobe was then carried out through very tenuous, avascular adhesions. Sharp dissection was necessary throughout. The

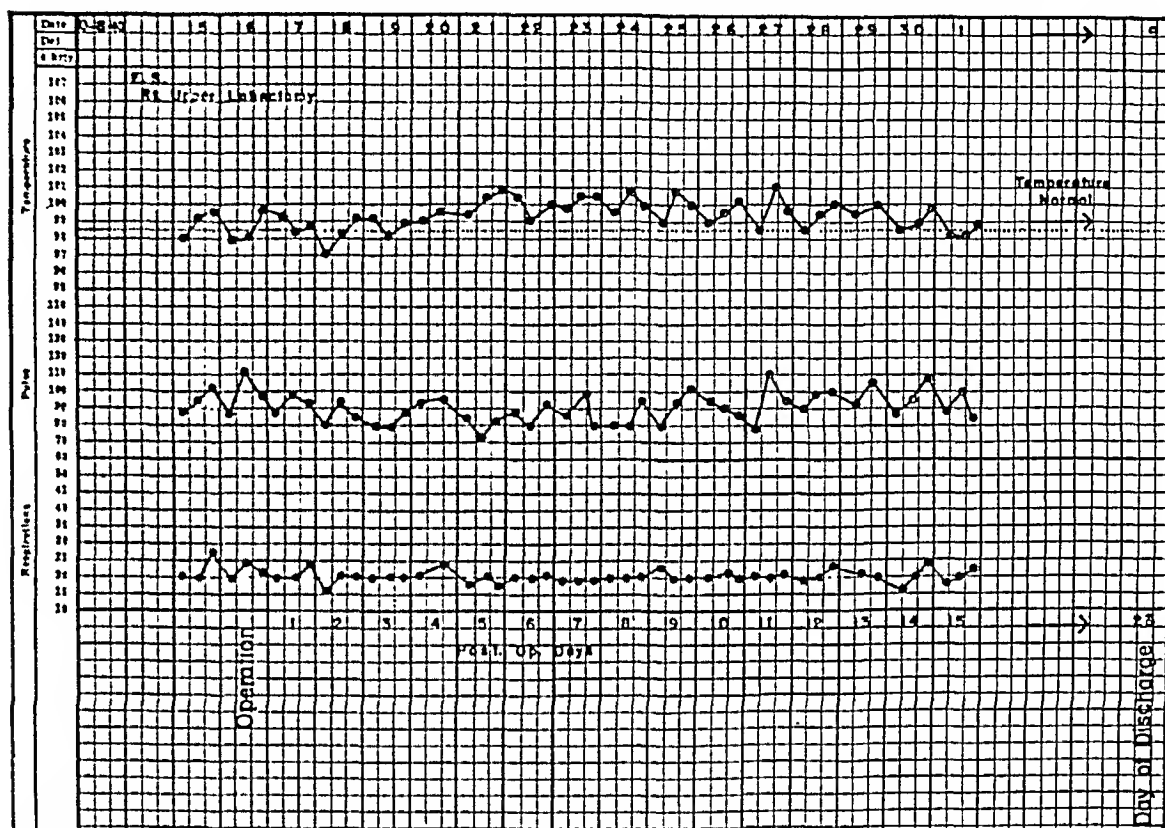


FIG. 5d.—Postoperative chart.

fissure between the lower and upper lobes of the left lung was identified and developed. On the posterior upper aspect of the lobe, considerable difficulty was met in freeing the lung from adhesions. The hilum of the lung was approached and individual ligation of the arteries and veins carried out. The fissure between the upper and lower lobes was then completed by cutting between clamps and suturing the defect. The bronchus to the left upper lobe was identified, two stay-sutures inserted and the bronchus divided. The bronchus was then closed with multiple interrupted silk sutures. The left lower lobe was then partially mobilized and a pedicle sutured over the closed bronchus. The specimen removed contained left upper lobe and lingula. Four grams of sulfanilamide were dusted into the pleural cavity, and the chest closed in layers, the divided muscles and skin being approximated with silk. The patient left the operating room in good condition, blood pressure being 110/80, and her blood well oxygenated.

Pathologic Examination.—*Gross:* (Fig. 6d): A shrunken left upper lobe. The pleural surface is roughened by the presence of fibrous tags representing old adhesions. The major bronchi have thickened walls and narrowed lumens. At the very apex there are several foci which hold inspissated caseous debris, and have sharply defined walls. They represent either previous cavities or old round foci, the latter are the

FIG. 5e.



FIG. 5f.

FIG. 5e. (Above)—Postoperative eight weeks (December 11, 1942): The right side is without visible tuberculous pathology. The left side exhibits two thin-walled small cavities, without the perifocal infiltration seen in the immediately preoperative film. No signs of postoperative exacerbation.

FIG. 5f. (Below)—Postoperative roentgenogram (December 30, 1942): Marginal artificial pneumothorax induced on left. Cavities no longer visible.

LOBECTOMY FOR TUBERCULOSIS

more probable. In the midportion of the lobe a few more foci are seen, the contents of which are caseous and firm. These, too, are well encapsulated but one presents a possible caseous breaking within the capsule. At the base of the lobe linear caseous stripes are seen representing traces of caseous bronchitis. The upper part of the lobe contains considerable fibrosis; the lower part is partially atelectatic. Both the distribution and the morphology of the caseous foci and the clinical course suggest very strongly an hematogenous origin of the process.

Postoperative Course.—Postoperative course was uneventful except that the patient

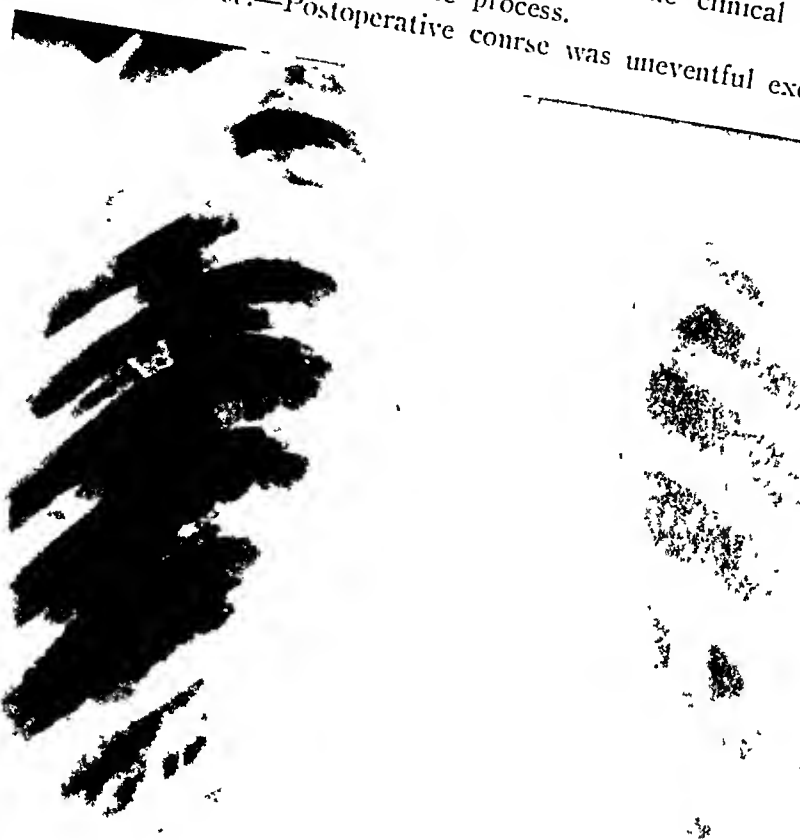


FIG. 6a.—May, 1936: Productive well circumscribed foci, no visible cavitation. Sputum positive for tuberculosis. Pneumothorax induced.

developed a transient pleural effusion which resorbed again within a few weeks. Patient was discharged on the 30th postoperative day to the Channing Home (Fig. 6e). *Postoperative Roentgenologic Examination.*—I-15-43: Showed a completely re-expanded left lower lobe, with a probable small effusion in the apex of the pleural space (Fig. 6f). Although the patient's general condition is good, her sputum has remained positive. Bronchoscopic examination on March 12, 1943, revealed narrowing and irregular proliferation of the left main bronchus with a 5 mm. ulceration.

COMMENT: The clinical significance of this case resides in the problem of cavity healing. Considering the complexity of questions and factors involved, the problem is proposed rather than discussed at this time. Cavity healing has been studied in recent years by Auerbach, Pagel, Pinner and others. According to these studies three anatomic forms of healed cavities can be differentiated: 1. The solid focus due to retention, inspissation, and final calcification of the cavity contents. 2. Radiating scar. 3. The bron-

chiectatic area remaining after the substitution of caseous and tuberculous elements in the cavity wall by ordinary granulation tissue, with subsequent epithelization and fibrous shrinking of the space. Healing by conversion of the cavity into a solid focus seems to be the most frequent form of cavity healing. It is noteworthy that the cases studied, the number of which is too small (16) to permit of a statistical analysis, were almost without exception obtained from individuals previously treated with some form of collapse therapy. In other words, collapse therapy, pneumothorax and thoracoplasty



FIG 6b—August, 1936 Incomplete artificial pneumothorax.

alike, may favor the conversion of the open cavity into a closed one that may still maintain a caseous focus.

We have been fortunate in being able to carry on careful studies on a relatively large number of surgically removed lobes and lungs. The specimens have all shown one type of cavity residuum, the so-called converted focus which, in clinical practice, is designated as "healed." These well walled-off foci, although firm in consistence, invariably contain caseous material. One or two in each specimen appear to be in the process of breaking through their capsules. It does not appear to be a permanent and safe method of cavity healing, yet it may well represent the characteristic response to collapse therapy.

LOBECTOMY FOR TUBERCULOSIS

The reliable type of cavity healing seems to be the concentric shrinking, with scarring. The two other types represent unrepaired damage to the lung, with a constant potentiality of reactivation or spread. These observations help explain the reluctance of the clinician to permit reexpansion of the lung after the disease appears to be under control with artificial pneumothorax. They also add weight to the proposal that irreparably damaged lobes be resected.

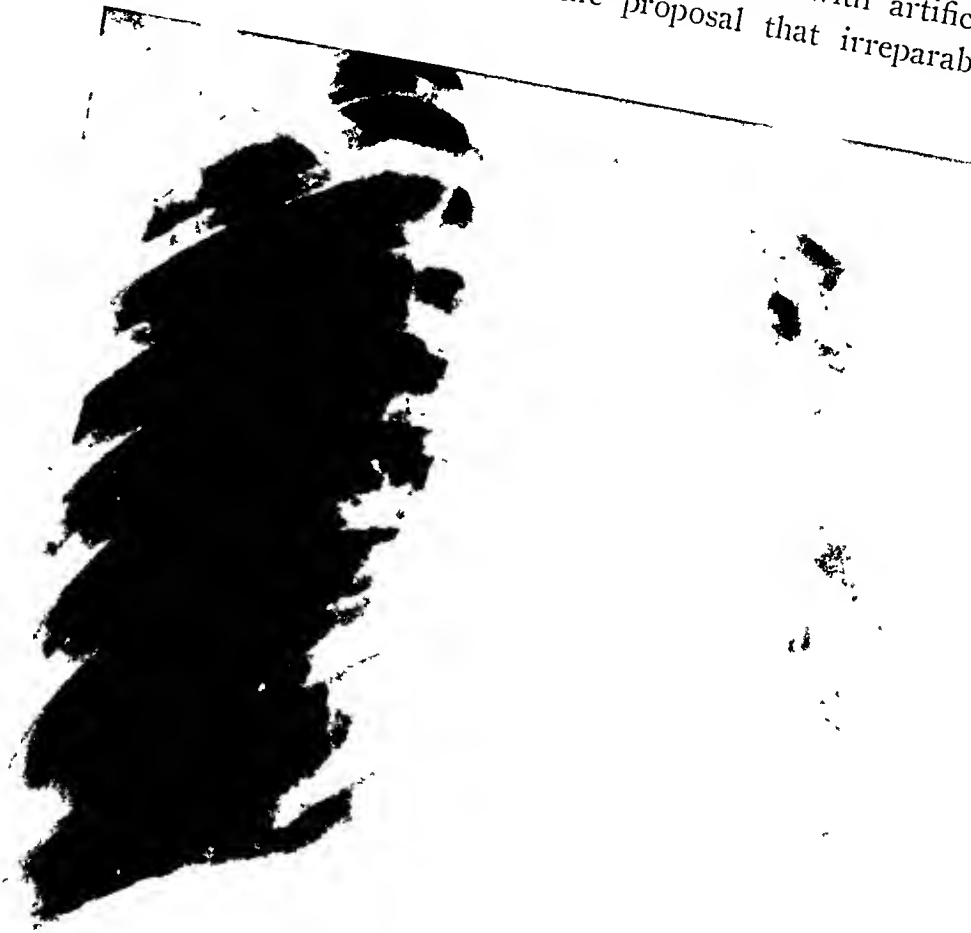


FIG. 6c.—Preoperative. The process present in the left upper lobe essentially unchanged compared with postpneumothorax roentgenograms, and with that from 1936.

TECHNICAL NOTES

Bronchoscopy: All patients were subjected to bronchoscopy preoperatively to rule out the presence of active ulceration in the trachea or stem bronchus.

Anesthesia: Gas-oxygen-ether administered through an intratracheal tube.

Incision: Posterolateral, with resection of a single rib at the appropriate level. An anteriorly placed incision would seem to impose unnecessary technical difficulties on the operator.

Dissection: In areas overlying densely adherent cavities the dissection is transferred from the intrapleural plane to the extrapleural plane. In looking for a fissure, however, one must be certain to return to the intrapleural plane. A layer of thickened parietal pleura will completely obscure the fissure. Meticulous hemostasis is maintained by ligatures and silver clips.

The frequently repeated statement that access to the hilum may be blocked by tuberculous infiltration of lymph nodes is erroneous. Once the primary lesion is established, tuberculous foci in an organ do not produce a lesion in the corresponding lymph nodes.¹ Upper (or lower) lobe lobectomy is carried out by individual ligation technic. An accurate knowledge of the complex anatomic structures and their common variations is essential.

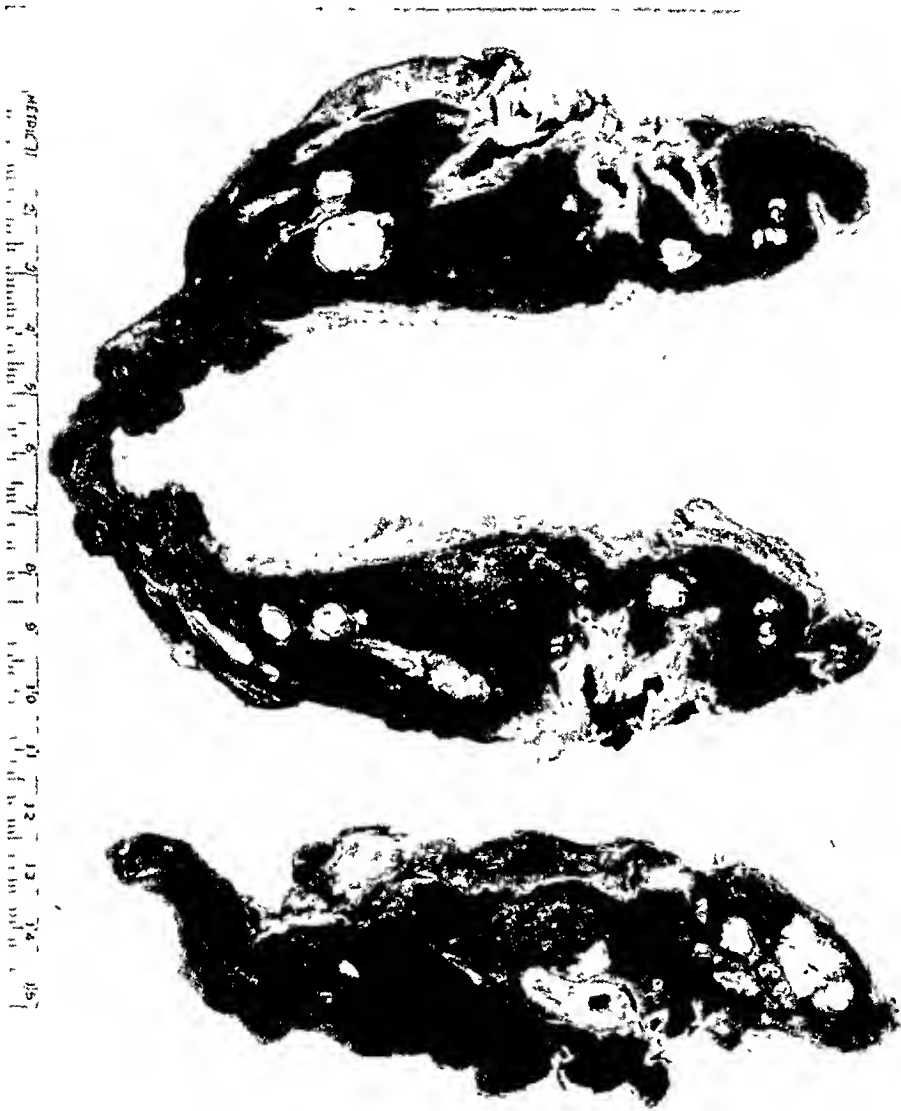


FIG. 6d.—Surgical specimen. Note the morphology and distribution of the foci. Traces of caseous bronchitis. (Pattern of hematogenous pulmonary tuberculosis.)

Following upper lobe resection the lower lobe, if adherent, is mobilized so that it may ascend to fill the apex. Intrathoracic crushing of the phrenic nerve has been done to reduce temporarily the volume of the hemithorax. Whether this is necessary or even advisable remains to be seen. In thoracoplasty one fears lower lobe aspiration pneumonitis in the presence of a paralyzed diaphragm. With surgical ablation of the source of sputum and complete freedom from paradoxical motion of the chest wall the conditions are quite different.

The pleural cavity is closed without drainage and the chest wall muscles approximated by interrupted sutures of fine silk. Intrapleural pressure is adjusted to a moderate degree of negative pressure.

Postoperative Care: An oxygen tent is used routinely for the first 24

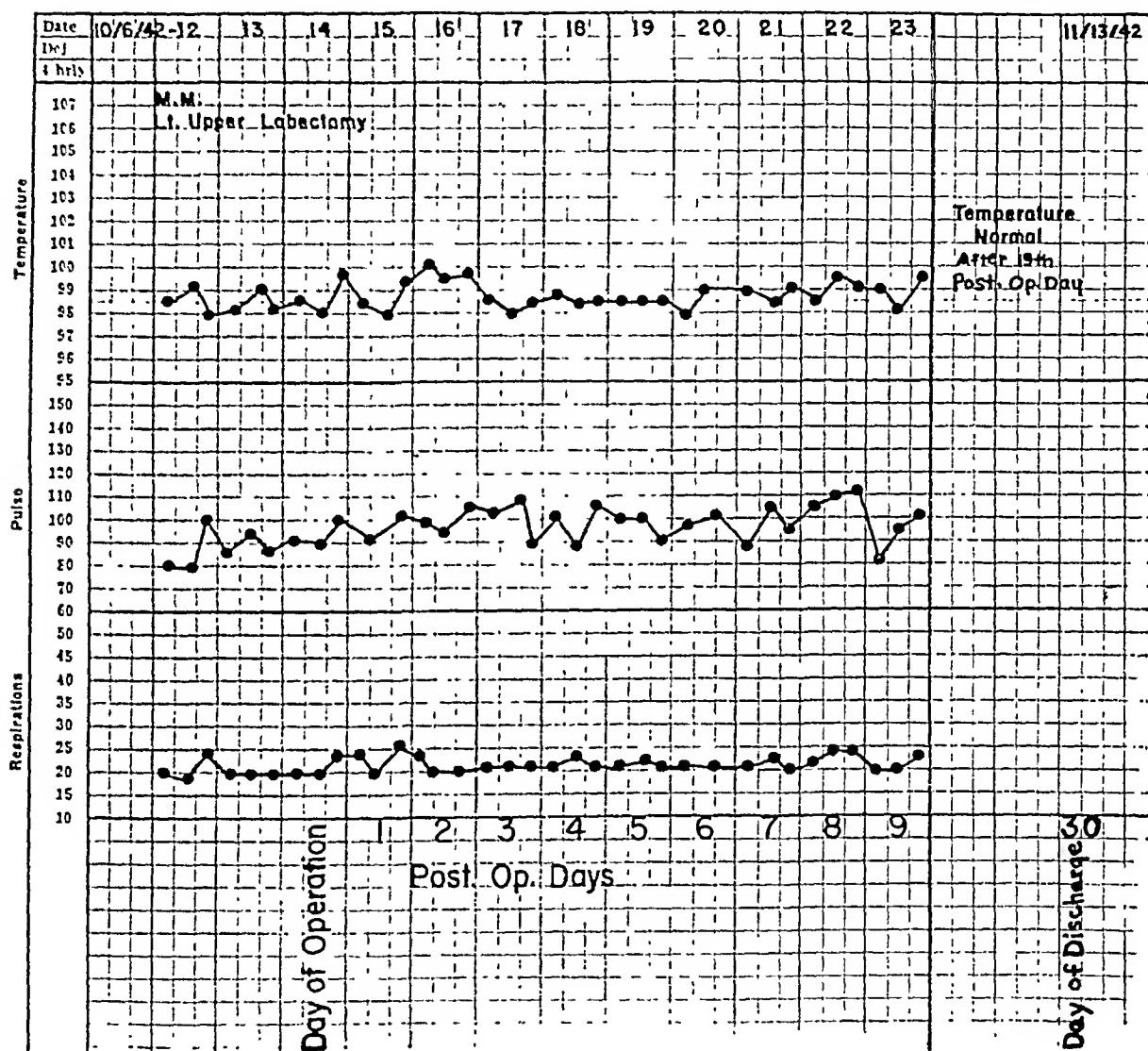


FIG. 6c.—Postoperative chart.

hours. Fluid or residual air may be reduced with needle aspiration, according to individual indications, preferably maintaining a moderate degree of negative pressure.

GENERAL COMMENTS: *If a lobectomy has been planned, technical difficulties that lead to resection of the entire lung must not be countenanced.* The goal of the operation is conservation of normal lung tissue as well as ablation of the diseased focus. Interlobar fissures that have been obliterated by adhesions, or anatomically incomplete fissures, *can and must be developed* by careful dissection. Discovery of healed foci in adjacent lobes is not an indication for resecting them.

From a technical standpoint total pneumonectomy is a more rapid and simple procedure than individual ligation lobectomy. Obviously, it has no place in this discussion as an alternative to artificial pneumothorax or thoracoplasty in dealing with unilobar tuberculosis.

DISCUSSION: Collapse therapy is eminently satisfactory in a high percentage of cases of pulmonary tuberculosis that require radical therapy. Its hazards are computable and by no means excessive. It has lightened but not eliminated the great economic and temporal wastage of the disease.

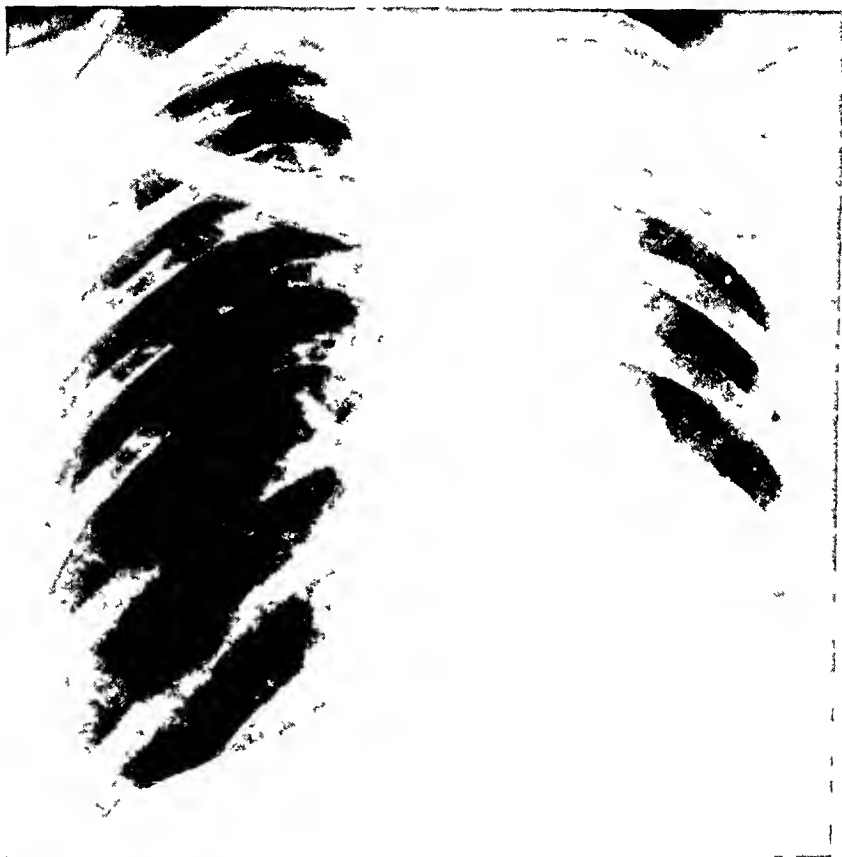


FIG 6f—Postoperative, January 15, 1943, three months after left upper lobectomy. There is one large and a few small calcifying foci visible in the apex of the reexpanded lower lobe but no active pathology discernible.

It may, for an indefinite period, remain the best form of treatment for the vast majority of patients requiring surgical intervention.

Before factual data are at hand to establish the safety of lobectomy as contrasted with thoracoplasty or long-continued artificial pneumothorax, it may seem mischievous to speculate regarding the theoretic advantages of such a procedure. A shortening of the span of treatment is not the least of these. Conversion of the personality all too frequently accompanies conversion of the sputum when the latter is attained at the expense of years of invalidism.

But from the more concrete physical point of view there are certain things to be gained. Lobectomy is more highly selective than thoracoplasty and as selective as the most skillfully managed pneumothorax, assuming in the

LOBECTOMY FOR TUBERCULOSIS

latter instance that healing and reexpansion are prohibited by the actual pathology. The functional capacity of the remaining lobe, or lobes, in the diseased side is preserved rather than encroached upon by long continued artificial pneumothorax or thoracoplasty.* The anatomic integrity of the thoracic cage and shoulder girdle remains essentially intact.

Most important of all, however, is the immediate ablation of the offending lesion in its entirety. This does not mean, of course, that the disease, tuberculosis, can be totally excised in many instances. While the open lesion under attack may represent only one manifestation of a generalized disease, there is reason to believe that its removal may aid rather than deleteriously affect remote latent or quiescent foci.

Surgeons familiar with tuberculosis will not need to be reminded that resection can only be considered after the patient's immunologic equilibrium has been restored by rest under a sanatorium regimen. Empyema, bronchial fistula, and implantation in the incision may otherwise be expected.

Artificial pneumothorax is in no way incompatible with subsequent lobectomy. When bed-rest alone is insufficient to bring the disease under control, pneumothorax or phrenic nerve paralysis may be added. If there is good reason to believe that the therapeutic goal of a reexpanded lung, with a closed lesion, cannot be achieved within a reasonable length of time, lobectomy may be considered when the acute phase has been brought under control.

CONCLUSIONS

Six cases of pulmonary tuberculosis are presented, three of which provided orthodox indications for resection of the lesion by lobectomy. Three others presented the usual indications for thoracoplasty but lobectomy was performed by election.

Healing *per primam* was the result in all instances.

Lobectomy provides a more selective and immediate method of eradicating certain lesions of tuberculosis than does collapse therapy. It may be used subsequent to artificial pneumothorax, thereby restoring to that procedure the reputation of finesse that it should enjoy.

A method of treatment that combines conservation of lung function, with immediate conversion of the sputum, and a shortening of the span of treatment, cannot be dismissed until its scope has been more fully explored.

REFERENCES

- ¹ Kayne, George Gregory, Pagel, Walter, and O'Shaughnessy, Laurence: *Pulmonary Tuberculosis: Pathology, Diagnosis, Management and Prevention*. Oxford University Press, London, New York, Toronto, 1939.
- ² Kent, Edward M., and Blades, Brian: *The Surgical Anatomy of the Pulmonary Lobes*. Jour. Thor. Surg., 12, 18, October, 1942.
- ³ Thornton, T. F., Jr., and Adams, W. E.: *The Resection of Lung Tissue for Pulmonary Tuberculosis*. Surg. Gynec. & Obst., 75, 312, October, 1942.

* The apex of the lower lobe lies at the level of the fourth rib in the paravertebral gutter. Modern "apical" or "selective" thoracoplasties rarely spare the sixth rib, and usually extend to include the seventh.

THE LOCAL EFFECT OF SULFANILAMIDE, SULFATHIAZOLE AND SULFADIAZINE UPON HEMOLYTIC STAPHYLOCOCCUS AUREUS INFECTIONS OF THE PLEURAL CAVITY

ROLLIN A. DANIEL, JR., M.D., F. T. BILLINGS, M.D.,*

AND

RICHARD R. CRUTCHER, M.D.†

NASHVILLE, TENN.

FROM THE DEPARTMENTS OF SURGERY AND MEDICINE, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE,
NASHVILLE, TENN.

ALLBRITTEN, FLICK AND GIBBON¹ recently reported upon the use of sulfanilamide in patients subjected to lobectomy or total pneumonectomy. The patients were given the drug by mouth on the day preceding operation and administration was continued postoperatively. In seven patients treated in this manner, four developed empyema. In ten patients, sulfanilamide was also placed in the pleural cavity after excision of the diseased lobe or lung. Eight of these patients developed empyema. Individual ligation of the hilar structures was performed in six lobectomies, and in six other lobectomies mass ligation of the hilum was employed. Empyema occurred in four patients in each group. Burford and Graham² published their clinical experience with the use of sulfanilamide in the pleural cavity following the removal of one or more lobes of the lung. Individual ligation of the hilar structures was employed in eight patients, and in all of these the bronchus remained closed. None of these patients developed empyema. Mass ligation of the hilum was performed in 14 cases, and the bronchus subsequently opened in every patient. Empyema occurred in all of these patients. They believe that "where contamination at the time of operation is rather gross, but where the bronchus may be reasonably expected to remain closed, the drug very likely has value in preventing an empyema."

Kent and Graham³ reported experimental observations on the prevention of empyema in dogs, produced by contamination of the pleura with putrid pus obtained from patients with empyema. The material was placed in the pleural space through an intercostal incision and lung tissue was not removed. Six groups of experiments were performed, with four animals in each group. Two cubic centimeters of pus was placed in every animal. The first group of four dogs received no drug. All died of empyema. In the second group, four grams of sulfanilamide was also placed in the pleural space. The same amounts of sulfapyridine, sulfathiazole and sulfaguaindine were used

* Captain F. T. Billings, M.C., U. S. Army.

† Captain Richard R. Crutcher, M.C., U. S. Army.

The sulfanilamide and sulfathiazole used in this work were supplied by E. R. Squibb & Sons, New York.

The sulfadiazine used in this work was supplied by Lederle Laboratories, New York, and E. R. Squibb & Sons, New York.

in the third, fourth and fifth groups, respectively. In the sixth group, a mixture of one gram of each of the above drugs was placed into the chest of each animal. All of the 20 treated animals recovered, and no evidence of infection was found when they were autopsied three weeks later.

The experiments presented in this report were undertaken to determine the relative effectiveness of the more commonly used sulfonamide drugs when employed locally, following experimental pneumonectomy in dogs. The hemolytic *Staphylococcus aureus* was employed as the infecting organism.

TABLE I

RESULTS OF INJECTION OF 4 CC. OF A 24-HOUR BROTH CULTURE + 8 CC. AGAR COMPARED WITH THOSE AFTER TREATMENT WITH SULFATHIAZOLE

4 Cc. 24-Hour Broth Culture + 8 Cc. Agar				Sulfathiazole			
Controls: No Drug Used				0.3 Gm. Sulfathiazole Per Kg. Body Weight			
Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity	Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity
1	24 hours	Empyema	H. <i>Staph. aureus</i>	2	6 days	Massive pleural effusion (1000 cc.)	No growth
3	4 days	Empyema	H. <i>Staph. aureus</i>	4	6 days	No cause apparent	No growth
5	4 days	Empyema	H. <i>Staph. aureus</i>	6	14 days	Empyema	H. <i>Staph. aureus</i>
7	4 days	Empyema	H. <i>Staph. aureus</i>	8		Sacrificed: 2 months	No growth
9	4 days	Empyema	H. <i>Staph. aureus</i>	10		Sacrificed: 2 months	No growth
11	6 days	Empyema	H. <i>Staph. aureus</i>	12		Sacrificed: 2 months	No growth
				13		Sacrificed: 2 months	No growth
Total No. dogs: 6. Died of empyema: 6				Total No. dogs: 7. Died of empyema: 1			

EXPERIMENTAL PROCEDURES

Normal dogs were used which varied in weight from 6 to 14 kilograms. The left chest wall was shaved and prepared with soap and water, and iodine and alcohol. Intravenous nembutal anesthesia was administered. Intermittent insufflation of air was administered through an intratracheal catheter.

Strict aseptic precautions were observed throughout the operative procedure. An incision was made in the left sixth intercostal space. The ribs were spread apart by means of a self-retaining retractor. The pulmonary vessels were divided between transfixing ligatures of silk. The bronchus was divided obliquely, and closed with interrupted fine silk sutures. The bronchial stump was then covered with a piece of mediastinal pleura. The organisms and drugs were placed in the pleural space through the open wound. The retracted ribs were then brought together by means of two encircling, fine stainless steel wire sutures. The soft tissues were closed in layers with interrupted sutures of fine silk.

Animals which died less than 12 hours after operation are not included in this study.

The amount of infectious material required as a minimal lethal dose varied in different groups of experiments. The animals in Table I were operated upon in groups of two, organisms being placed into the chest of one dog and the organisms and drug into the other. Animals of approximately

the same weights were used in each of these groups. Four cubic centimeters of a 24-hour blood broth culture of hemolytic *Staphylococcus aureus*, mixed with eight cubic centimeters of warm agar, were used. Table II represents a group of 12 animals, all operated upon during the same day. Organisms of known virulence were in this way used in control animals and in animals in which sulfonamide therapy was used. Tables III and IV are groups of experiments carried out in the same way.

TABLE II

RESULTS OF INJECTION OF 0.25 CC. OF A 24-HOUR BROTH CULTURE COMPARED WITH THOSE AFTER TREATMENT WITH SULFANILAMIDE

0.25 Cc. 24-Hour Broth Culture				Sulfanilamide			
Controls: No Drug Used				0.3 Gm. Sulfanilamide Per Kg. Body Weight			
Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity	Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity
14	36 hours	Empyema	H. <i>Staph. aureus</i>	15	24 hours	Empyema	H. <i>Staph. aureus</i>
16	48 hours	Empyema	H. <i>Staph. aureus</i>	17	24 hours	Empyema	H. <i>Staph. aureus</i>
18	48 hours	Empyema	H. <i>Staph. aureus</i>	19	24 hours	Empyema	H. <i>Staph. aureus</i>
20	3 days	Empyema	H. <i>Staph. aureus</i>	21	2 days	Empyema	H. <i>Staph. aureus</i>
22	4 days	Empyema	H. <i>Staph. aureus</i>	23	5 days	Empyema	H. <i>Staph. aureus</i>
24	5 days	Empyema	H. <i>Staph. aureus</i>	25	Living (3 mos.)		
Total No. dogs: 6. Died of empyema: 6.				Total No. dogs: 6. Died of empyema: 5.			

TABLE III

RESULTS OF INJECTIONS OF 0.25 CC. OF A 24-HOUR BROTH CULTURE COMPARED WITH THOSE AFTER TREATMENT WITH SULFATHIAZOLE

0.25 Cc. 24-Hour Broth Culture.				Sulfathiazole			
Controls: No Drug Used				0.3 Gm. Sulfathiazole Per Kg. Body Weight			
Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity	Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity
26	36 hours	Empyema	H. <i>Staph. aureus</i>	27	5 days	Bronchus open. No infection	No growth
28	48 hours	Empyema	H. <i>Staph. aureus</i>	29	6 days	Pneumonia, rt. No pleural infection	No growth
30	3 days	Empyema	H. <i>Staph. aureus</i>	31	10 days	Not determined. No infection	No growth
32	3 days	Empyema	H. <i>Staph. aureus</i>	33		Sacrificed: 12 days. Wound disrupted. No infection	No growth
34	5 days	Empyema	H. <i>Staph. aureus</i>	35	Living (3 mos.)		
36	Living (3 mos.)			37	Living (3 mos.)		
Total No. dogs: 6. Died of empyema: 5.				Total No. dogs: 6. Died of empyema: 0.			

TABLE IV

RESULTS OF INJECTION OF 0.25 CC. OF A 24-HOUR BROTH CULTURE COMPARED WITH THOSE AFTER TREATMENT WITH SULFADIAZINE

0.25 Cc. 24-Hour Broth Culture				Sulfadiazine			
Controls: No Drug Used				0.3 Gm. Sulfadiazine Per Kg. Body Weight			
Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity	Exper. No.	Duration of Life after Op.	Cause of Death	Culture of Pleural Cavity
38	3 days	Empyema	H. <i>Staph. aureus</i>	39	24 hours	Empyema	H. <i>Staph. aureus</i>
40	3 days	Empyema	H. <i>Staph. aureus</i>	41	24 hours	Empyema	H. <i>Staph. aureus</i>
42	3 days	Empyema	H. <i>Staph. aureus</i>	43	24 hours	Empyema	H. <i>Staph. aureus</i>
44	4 days	Empyema	H. <i>Staph. aureus</i>	45	Living (3 mos.)		
46	5 days	Empyema	H. <i>Staph. aureus</i>	47	Living (3 mos.)		
48	5 days	Empyema	H. <i>Staph. aureus</i>	49	Living (3 mos.)		
Total No. dogs: 6. Died of empyema: 6.				Total No. dogs: 6. Died of empyema: 3.			

EFFECTS OF SULFONAMIDE THERAPY

In order to more definitely control the virulence of the organisms, experiments were performed upon 16 dogs with organisms which had been frozen at -78°C . (Table V). The organism was recovered from the pleural cavity of a dog with empyema. It was grown on large blood agar plates and washed from these plates with sterile normal saline solution after a growth-period of six hours. This suspension, thoroughly mixed, was placed in sterile pyrex ampules. The ampules, containing from one to two cubic centimeters of the suspension, were sealed by heat and placed immediately into 95 per cent alcohol in the freezing compartment. One cubic centimeter of this suspension contained approximately five billion bacteria.

TABLE V
RESULTS OF INJECTION OF 0.02 CC. (ABOUT 100 MILLION) OF FROZEN ORGANISMS COMPARED WITH THOSE AFTER TREATMENT WITH SULFANILAMIDE, SULFATHIAZOLE AND SULFADIAZINE
Frozen Organisms (In Saline Suspension): 0.02 Cc. (About 100 Million)

	Sulfanilamide 0.3 Gm. Per Kg. Body Weight	Sulfathiazole 0.3 Gm. Per Kg. Body Weight	Sulfadiazine 0.3 Gm. Per Kg. Body Weight
Control: No Drug Used			
1.....Died 20 hours. Empyema. Culture: <i>H. Staph. aureus</i>	Died 4 days Empyema Culture: <i>H. Staph. aureus</i>	Sacrificed 15 days. No infection. Culture: No growth	Living (2 months)
2.....Died 5 days. Empyema. Culture: <i>H. Staph. aureus</i>	Died 6 days. Empyema-Wound disruption. Culture: <i>H. Staph. aureus</i>	Died 6 days. Wound disruption. No infection. Culture: No growth	Sacrificed 15 days. No infection. Culture: no growth
3.....Died 4 days. Empyema. Culture: <i>H. Staph. aureus</i>	Sacrificed 14 days. No infection. Culture: No growth.	Died 5 days. Wound disruption. No infection. Culture: No growth	Living (2 months)
4.....Sacrificed 14 days. No infection. Culture: No growth	Died 12 hours. Small amount fluid. Culture: <i>H. Staph. aureus</i>	Died 3 days. Empyema. Culture: <i>H. Staph. aureus</i>	Died 4 days. Empyema. Culture: <i>H. Staph. aureus</i>
Total No. dogs....	4	4	4
Total No. dead of empyema	3	3	1

TABLE VI
FATE OF ENTIRE GROUP OF DOGS INNOCULATED WITH MINIMAL LETHAL DOSE OF HEMOLYTIC STAPHYLOCOCCUS AUREUS FOLLOWING PNEUMONECTOMY

	Died of Empyema	Died of Other Cause	No Empyema	Lived	Total No. Dogs	Per Cent Dying of Empyema
Controls: No drugs used.....	26	0	0	2	28	92.9 per cent
Sulfanilamide 0.3 Gm. per Kg. body weight..	8	0	0	2	10	80.0 per cent
Sulfathiazole 0.3 Gm. per Kg. body weight..	2	8	0	7	17	11.8 per cent
Sulfadiazine 0.3 Gm. per Kg. body weight..	4	0	0	6	10	40.0 per cent

In Table VI the animals were operated upon in groups of four. Two-hundredths of a cubic centimeter of the organism suspension was placed in the pleural cavity of each dog. One animal was used as a control and the other three were subjected to the intrapleural application of sulfanilamide, sulfathiazole and sulfadiazine.

Pneumonectomy was performed upon 14 dogs which were not contaminated with the organisms. The effect of the sulfonamides upon the pleura were noted in 11 of these animals.

Sulfanilamide, sulfathiazole and sulfadiazine are the drugs which were employed. Three-tenths of a gram per kilogram of body weight was chosen as the amount of drug to be used in all experiments. Finely powdered crystals of the drug were poured through the wound over the surface of the mediastinal pleura immediately after introduction of the organisms.

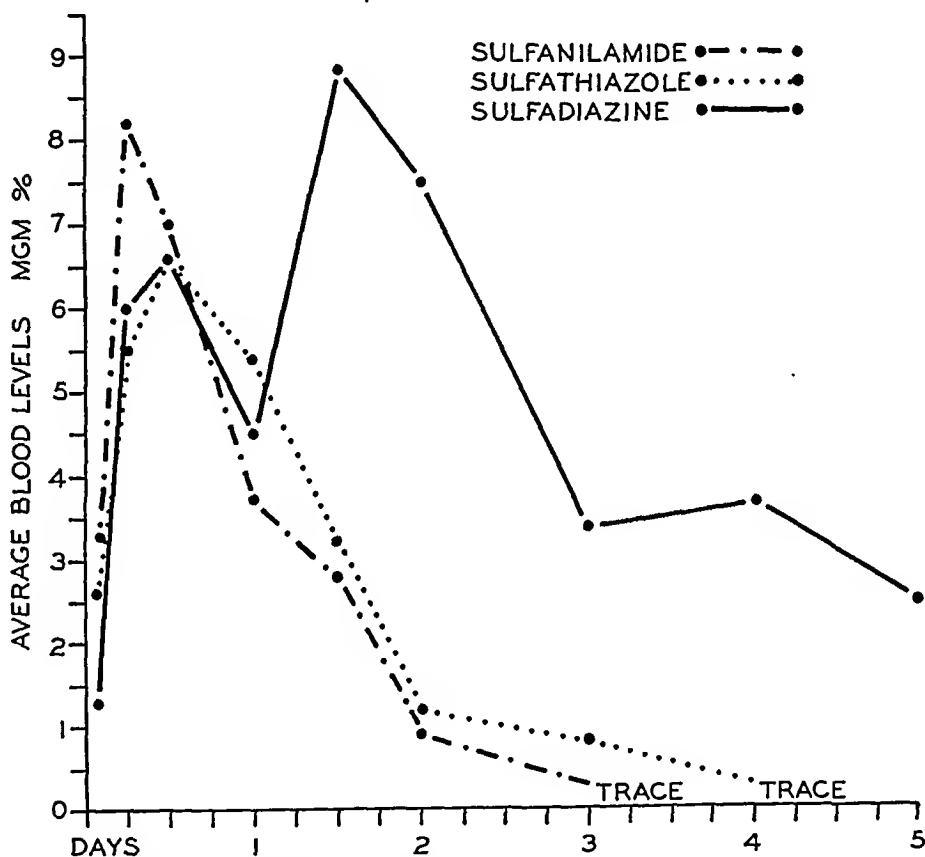


CHART 1.—Graphic representation of the effects of sulphonamide therapy on the blood concentration. (Recorded in milligrams per 100 cc. of blood.)

The blood concentration determinations were recorded in milligrams per 100 cc. of blood, according to the method of Bratton and Marshall.⁴ Average blood levels were computed, and are shown in Chart 1. These determinations were all made from animals contaminated with the organisms. The sulfanilamide and sulfadiazine curves represent average levels from five animals each, the sulfathiazole curves from eight animals.

RESULTS

THE EFFECT OF THE SULFONAMIDES ON THE PLEURA

Left total pneumonectomy was performed upon 11 dogs in which 0.3 Gm. of sulfonamide drug per Kg. of body weight was placed in the pleural

EFFECTS OF SULFONAMIDE THERAPY

space. The animals tolerated the procedure well. They were sacrificed and examined at intervals after operation, with the following results:

Sulfanilamide.—Three dogs: Sacrificed on the fourth, eleventh and forty-fifth days after operation. The pleura was clean and glistening in all. The pleural space was obliterated in the last animal, and there were a few adhesions present between the scar of the old wound of the chest wall and the mediastinal pleura. There was no fluid or drug present.

Sulfathiazole.—Five dogs: Sacrificed on the fourth, sixth, eighth and eleventh days. In the first, scattered small deposits of the drug were seen. The pleura was moist and glistening in all, and free fluid was not present. The fifth dog was autopsied four months after operation. The pleural space was obliterated and there were adhesions between the mediastinum and the scar of the chest wall. There was no fusion elsewhere.

Sulfadiazine.—Three dogs: Sacrificed five and sixteen days and ten weeks after operation. In the first, there were many fibrinous adhesions between the mediastinum and the pleura of the chest wall. Thirty cubic centimeters of thin bloody fluid and extensive scattered deposits of sulfadiazine were present. In the second, there were no adhesions, fluid or drug present. In the third animal there were many dense fibrous adhesions binding the mediastinal pleura to the lateral chest wall. No fluid or drug was present.

The appearance of the pleural space following the application of sulfanilamide and sulfathiazole was exactly comparable to three dogs subjected to pneumonectomy, in which no drug was placed in the pleural cavity. Evidence of definite and more violent inflammatory reaction followed the administration of sulfadiazine.

THE PREVENTION OF HEMOLYTIC STAPHYLOCOCCUS AUREUS INFECTIONS

The tables are arranged in the order in which the experiments were performed.

Sulfathiazole was the most effective of the three sulfonamides in the prevention of fatal empyema. Sulfadiazine appears to have been almost as efficacious as sulfathiazole. Sulfanilamide offered the least protection against the infection.

Cultures of the heart's blood were obtained from two animals (one control and one treated animal) in each group which died of empyema. These cultures all remained sterile.

The maintenance of a high blood level of sulfadiazine for a period of five days is interesting. It should be noted that sulfanilamide and sulfathiazole disappeared from the blood stream in nearly the same period of time after operation despite the difference in the occurrence of fatal empyema in the two groups of animals.

Disruption of the chest wound occurred in three animals in the sulfathiazole group and in one in which sulfanilamide was used. The wound was

not disrupted in any of the control animals (28 dogs) although all but two developed fatal empyema.

SUMMARY AND CONCLUSIONS

1. The effects of sulfanilamide, sulfathiazole and sulfadiazine upon the pleural cavity following pneumonectomy has been studied in the dog.

2. The local effects of sulfanilamide, sulfathiazole and sulfadiazine upon the prevention of hemolytic staphylococcus infection in the pleural cavity of the dog, following pneumonectomy, have been studied.

3. There is little gross local evidence of reaction to sulfanilamide or sulfathiazole used in the pleural cavity following pneumonectomy. Sulfadiazine produces a more marked inflammatory reaction than do the other drugs.

4. The local use of sulfathiazole is more effective in preventing hemolytic staphylococcus empyema following pneumonectomy in the dog than are either sulfanilamide or sulfadiazine. The local use of sulfanilamide is least effective in prevention of this infection.

5. The absorption of sulfanilamide from the contaminated pleural cavity takes place slightly more rapidly than does sulfathiazole. The absorption of sulfadiazine occurs much more slowly than either of the other drugs.

6. A greater incidence of wound disruption in animals in which sulfathiazole was used suggests that this drug may have interfered with the healing of the wounds.

REFERENCES

- ¹ Allbritten, F. F., Flick, J. B., and Gibbon, J. H., Jr.: The Use of Sulfanilamide in Partial and Total Resection of the Lung. *J. Thor. Surg.*, **11**, 187, 1941.
- ² Burford, T. H., and Graham, E. A.: The Local Use of Sulfanilamide in the Pleural Cavity. *J. Thor. Surg.*, **11**, 203, 1941.
- ³ Kent, E. M., and Graham, E. A.: Experimental Observations on the Use of Drugs of the Sulfonamide Group in the Pleural Space. *J. Thor. Surg.*, **11**, 198, 1941.
- ⁴ Bratton, A. C., and Marshall, E. K., Jr.: A New Coupling Component for Sulfanilamide Determinations. *J. Biol. Chem.*, **128**, 537, 1939.

THE EFFECT OF SULFANILAMIDE, SULFATHIAZOLE AND SULFADIAZINE UPON THE PERITONEUM

RICHARD R. CRUTCHER, M.D.,* ROLLIN A. DANIEL, JR., M.D.,
AND
F. T. BILLINGS, M.D.†

NASHVILLE, TENN.

FROM THE DEPARTMENTS OF SURGERY AND MEDICINE, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE,
NASHVILLE, TENN.

THE INTRAPERITONEAL use of the sulfonamides is now practiced widely for the treatment and prevention of infection. Sulfanilamide has been most frequently used and is said not to produce any evidences of foreign body reaction. Harbison and Key¹ implanted large doses of sulfanilamide, sulfathiazole and sulfadiazine (500 mg.) into the abdominal cavities of rats and found no evidence of inflammatory reaction to any of these drugs or to mixtures of sulfanilamide and sulfathiazole after 28 days.

Jackson and Collier² present a series of experiments carried out on dogs, sulfanilamide being implanted and peritoneal fluid being examined for cellular response. The peritoneal cavities were examined from four hours to one month later. They found no evidence of reaction to the drug. In the discussion of this article Ochsner stated that sulfanilamide produces intense inflammation in the abdominal wounds of patients, and this opinion was emphasized by Collier.

Laird and Stavern³ performed 11 experiments on seven dogs, sulfanilamide being implanted in three dogs, sodium sulfathiazole in four and, later, sulfathiazole in the first three. Evidence of marked inflammation was noted after the use of sodium sulfathiazole, none in the other experiments. One-half gram of each drug per kilogram of body weight was used and the dogs were examined at the end of two, four and eight weeks.

The articles of Ravdin, Rhoads and Lockwood,⁴ Muller and Thompson,⁵ and of Jackson and Collier,² are illustrative of the improved clinical results which are attributed to the local use of the sulfonamides in the treatment of peritonitis.

The experiments presented in this report were undertaken preparatory to the experimental study of the effect of the sulfonamides on infections of the peritoneal cavity.

* Captain Richard R. Crutcher, M.C., U. S. Army.
† Captain F. T. Billings, M.C., U. S. Army.

The sulfanilamide and sulfathiazole used in this work were supplied by E. R. Squibb & Sons, New York.

The sulfadiazine used in this work was supplied by Lederle Laboratories, New York, and E. R. Squibb & Sons, New York.

METHOD OF STUDY

Fifty-five dogs were used. The effect of sulanilamide, sulfathiazole and sulfadiazine placed in the peritoneal cavities was determined. It was noted prior to these experiments that when finely powdered crystals of sulfathiazole were poured into the peritoneal cavities of dogs, a part of the drug tended to become "walled-off" by the omentum into a mass or lump, which when removed was often quite hard, and when this occurred a part of this lump might remain for as long as four days. It was also noted that when very finely powdered drug was used this tendency to form lumps was more marked than when coarse crystals were used. When this occurred adhesions between loops of intestine were more apt to be found later. Attention has been directed to this by Throckmorton,⁷ in a thorough study of the cellular response to various drugs in the peritoneal cavity of the albino rat.

The method of introduction of the drug was varied as follows: In one group finely powdered crystals of the drug were scattered about over the loops of intestine. In a second group, the drug was suspended in about 50 cc. of sterile distilled water, and this was poured through the wound among the loops of intestine. In the third group, a weighed amount of drug was moistened with distilled water and then allowed to dry. In this way a hard lump of the drug was formed. This was broken into four or five pieces and these lumps were placed among the loops of intestine.

In all experiments 0.3 Gm. of drug per kilogram of body weight were used.

The drug was introduced through a short right paramedian abdominal incision, under intravenous nembutal anesthesia. The operation was performed under aseptic conditions. The omentum was delivered through the wound and the small bowel was carefully examined for the presence of adhesions. After the omentum was replaced in the abdominal cavity the wound was closed in layers with interrupted fine silk sutures.

The abdomen was reopened at varying periods of time after the introduction of the drugs. In some instances this was done after the animal was sacrificed. In others a left paramedian incision was made under nembutal anesthesia and under aseptic conditions, the entire intestinal tract was carefully examined and the incision closed. These animals were then examined again later.

In none of the experiments included in this study was there any evidence of infection of the wound or the peritoneum postoperatively.

The blood content of the drugs was determined at intervals of several hours after the original operation, by method of Bratton and Marshall.⁶

RESULTS

Four animals were operated upon in which the intestines were examined but no drug was introduced. Later examination (5-14 days after operation) showed no adhesions or other evidences of inflammation.

EFFECTS OF SULFONAMIDE THERAPY

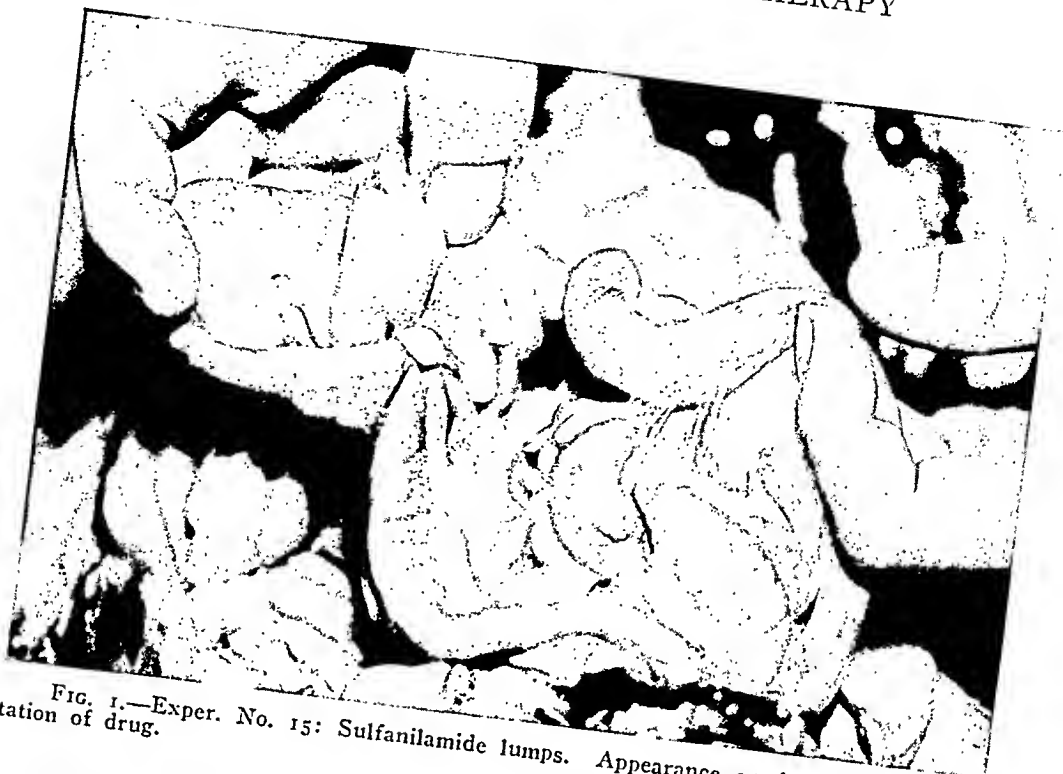


FIG. 1.—Exper. No. 15: Sulfanilamide lumps. Appearance 35 days after implantation of drug.

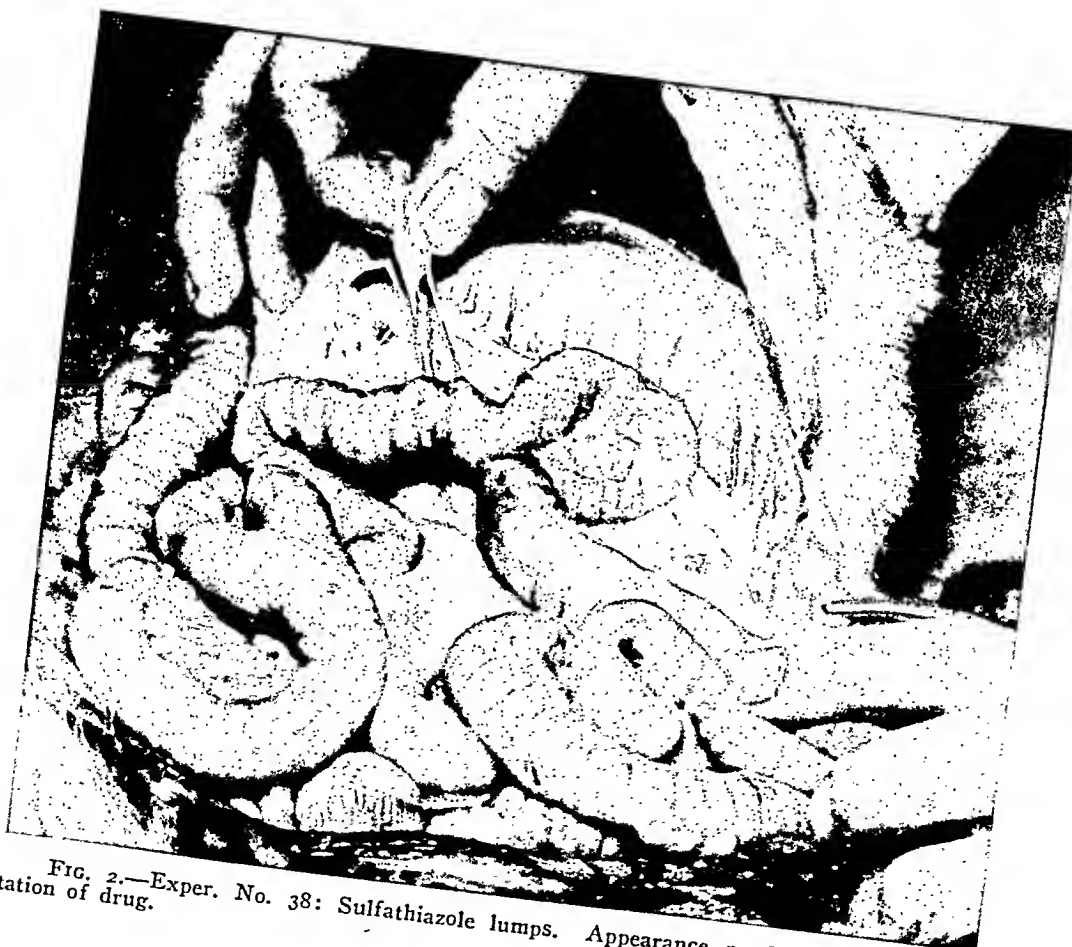


FIG. 2.—Exper. No. 38: Sulfathiazole lumps. Appearance 54 days after implantation of drug.



FIG. 3.—Exper. No. 40: Finely powdered sulfadiazine. Appearance 45 days after implantation of drug.



FIG. 4.—Exper. No. 43: Suspension of sulfadiazine. Appearance 35 days after operation.

EFFECTS OF SULFONAMIDE THERAPY

TABLE I
FINELY POWDERED CRYSTALS

Exper. No.	Time of Examination after Drug Implantation	Number and Character of Adhesions	Visible Drug Remaining
Sulfanilamide.... 1	5 days	None	None
2	5 days & 36 days	Slight 5 days; none 36 days	None
3	5 days & 66 days	None	None
4	11 days	None	None
5	98 days	None	None
Sulfathiazole.... 18	4 days	None	None
19	5 days & 6 months	None	None
20	6 days	None	None
21	9 days & 31 days	None	None
22	11 days	Marked 9 days; slight 31 days	None
23	22 days	None	None
24	13 days & 91 days	None	None
25	13 days	None	None
26	13 days	Slight 13 days; none 91 days	None
27	9 days	None	None
28	13 days	Slight	None
Sulfadiazine 39	10 days	None	None
40	8 & 45 days	None	None
41	10 & 45 days	Marked: 8 & 45 days	None
42	8 & 45 days	Marked: 10 & 45 days	Several small lumps, 8 days
		Marked: 8 & 45 days	1 small lump, 8 days

TABLE II
FINELY POWDERED CRYSTALS SUSPENDED IN STERILE DISTILLED WATER (ABOUT 50 CC.)

Exper. No.	Time of Examination after Drug Implantation	Number and Character of Adhesions	Drug Remaining
Sulfanilamide.... 6	4 days	None	None
7	4 days	2 small (omentum-bowel)	None
8	7 days	None	None
9	7 days	None	None
10	7 days	None	None
11	11 days	None	None
Sulfathiazole.... 29	9 & 31 days	Slight 9 days; none 31 days	None
30	9 & 31 days	None	None
31	9 & 31 days	None	None
32	9 & 31 days	Slight: 9 & 31 days	None
33	9 & 31 days	Slight: 9 & 31 days	None
Sulfadiazine..... 43	6 & 36 days	Marked: 6 & 36 days	None
44	6 & 36 days	Moderate: 6 & 36 days	None
45	12 days	Moderate	None
46	12 days	None	None
47	20 days	None	None
48	28 days	None	None
49	28 days	None	None

TABLE III
LUMPS

Exper. No.	Time of Examination after Drug Implantation	Number and Character of Adhesions	Drug Remaining
Sulfanilamide.... 12	9 days	Moderate	None
13	9 days & 34 days	Moderate	None
14	9 days & 34 days	Moderate	None
15	9 days & 34 days	Moderate	None
16	8 days	None	Small lump at 9 days
17	28 days	None	None
Sulfathiazole.... 34	5, 62 & 91 days	Marked: 5, 62 & 91 days	None
35	3 & 37 days	Moderate 3 days; none 37 days	1 large lump at 5 days
36	12 days	Moderate	4 small at 3 days
37	20 days	Moderate	None
38	37 days	Moderate	None
Sulfadiazine..... 50	20 days	Marked	2 small lumps
51	20 days	Marked	1 large lump
			None

The findings in the peritoneal cavities of the animals are summarized in Tables I, II and III. The persistent evidence of peritoneal reaction was based upon the presence of adhesions existing between the omentum and the bowel, but adhesions between the scar of the wound of the abdominal wall and the omentum or the viscera were disregarded. The reaction was graded as follows: "Slight," indicating the presence of from one to four narrow or filmy adhesions; "moderate," indicating the presence of several dense bands of adhesions; and "marked," indicating widespread dense adhesions.

There was evidence of peritoneal reaction in at least one animal in all of the groups of experiments. The adhesions first noted after the use of fine crystals of sulfanilamide and sulfathiazole had disappeared when the animals were examined later, with the possible exception of Exper. No. 27. This animal was sacrificed on the ninth postoperative day. In Exper. No. 7 (sulfanilamide in suspension), the dog was sacrificed on the fourth day. It is probable that the two small adhesions noted there would have subsequently disappeared. With the exception of this one experiment, no adhesions were noted after the use of sulfanilamide in suspension, whereas adhesions were present nine days after operation in three out of five animals used in the sulfathiazole suspension group, and these adhesions persisted in two animals for 31 days.

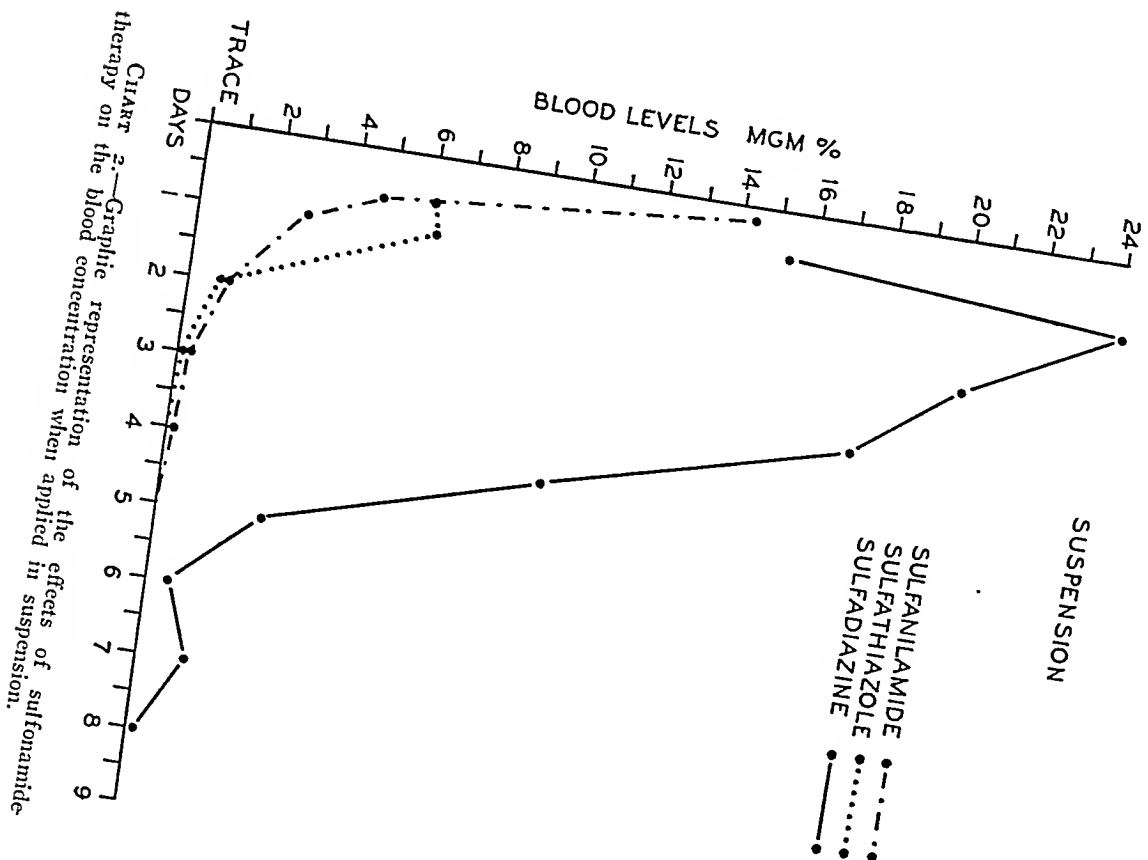
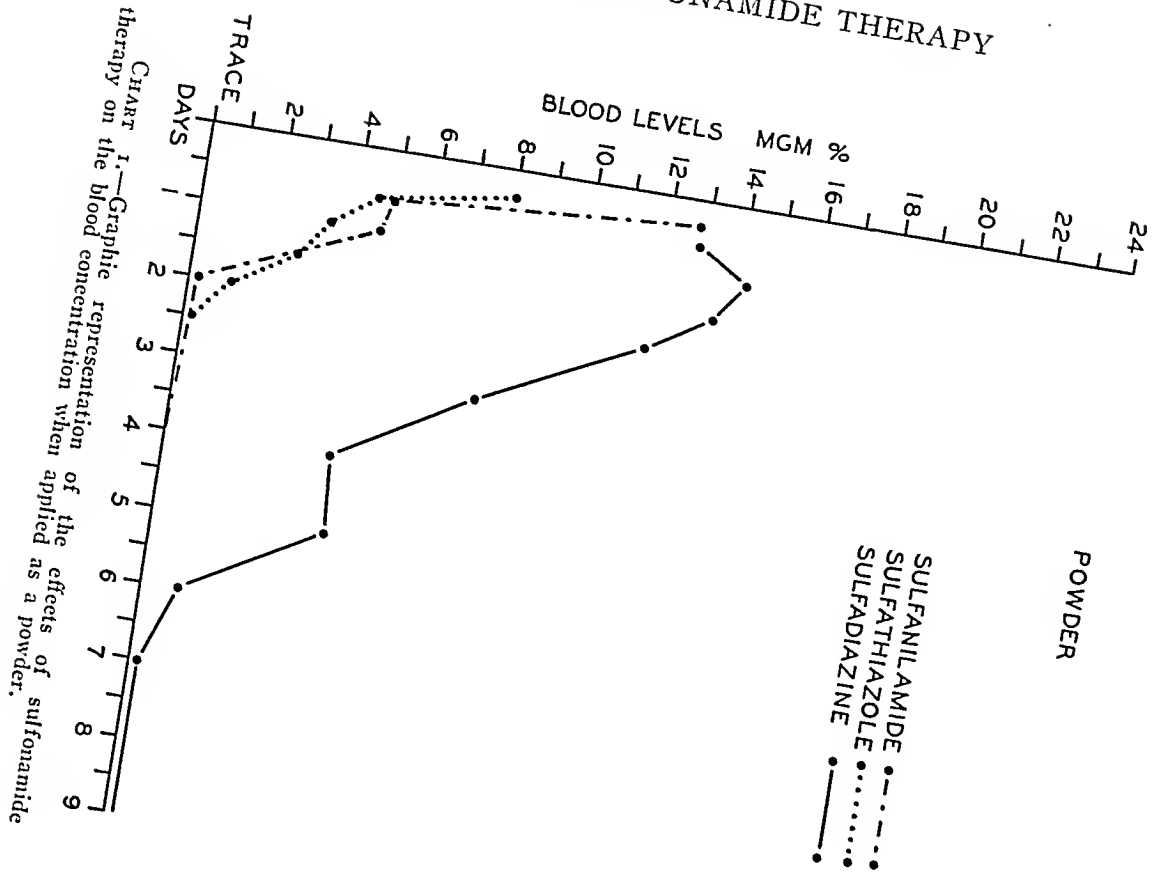
When lumps of the drug were used the reaction was similar to that which is seen to occur about any foreign material. Moderate to marked adhesions were formed which persisted, but the reaction was less marked with sulfanilamide than with the other drugs.

Numerous adhesions occurred following the use of sulfadiazine in all three groups of experiments, but they appeared to be less marked when the suspension was used.

When lumps were used, small portions of the drug were occasionally still present several days after they were introduced. Two small lumps of sulfathiazole were found in the center of a mass of adhesions 37 days after operation and a large mass of sulfadiazine was found 20 days after.

The average blood levels of the drugs were computed for each group, and these average curves are shown in Charts 1, 2 and 3. As might be expected, sulfanilamide was absorbed rapidly and remained in the blood stream for a shorter period of time than did the other drugs. A considerably higher concentration of the drug was obtained with sulfadiazine than with the other drugs. A correlation of absorption rate and the local evidences of reaction to the different drugs is possible, and it may be that the absence of severe reaction to the implantation of sulfanilamide is due to the ability of the animal to rapidly absorb and excrete the drug. Sulfadiazine might be expected to be most beneficial in the treatment or prevention of infection because of its slow absorption rate and persistent high local concentration. On the other hand, it produces evidence of considerable damage to the tissues, possibly by persisting longer as foreign material.

EFFECTS OF SULFONAMIDE THERAPY



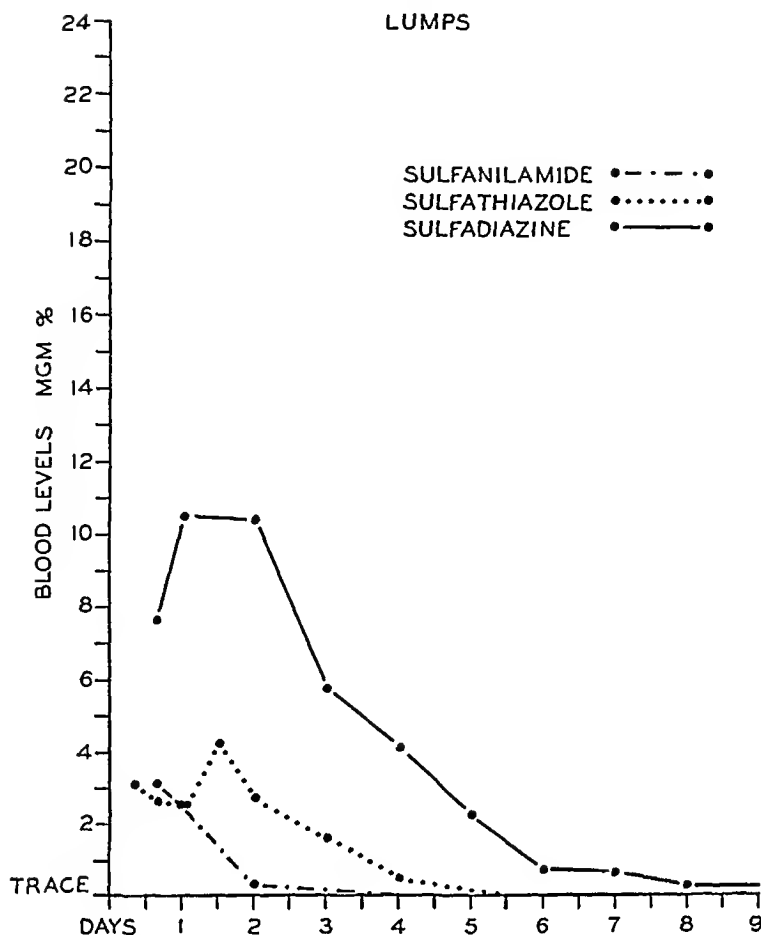


CHART 3.—Graphic representation of the effects of sulfonamide therapy on the blood concentration when applied in lumps.

CONCLUSIONS

1. Sulfanilamide, sulfathiazole and sulfadiazine may all produce adhesions within the peritoneal cavity of the dog under certain conditions. These adhesions may be persistent for long periods of time.

2. Masses of the drugs are apt to become "walled-off" as a foreign body and be absorbed very slowly.

3. Care should be taken to distribute the finely powdered drug evenly about the available surface of the peritoneum to avoid the formation of lumps. This may be easily accomplished by introducing the drug in a suspension of sterile water or saline.

4. Sulfadiazine produces much greater local reaction than sulfanilamide or sulfathiazole.

5. The absorption of sulfadiazine from the peritoneal cavity occurs more slowly than does the absorption of sulfanilamide or sulfathiazole.

REFERENCES

- 1 Harbison, S. P., and Key, J. A.: Local Implantation of Sulfanilamide and its Derivatives in Wounds: Its Relation to Wound Healing and to Peritoneal Adhesions. *Arch. Surg.*, 44, 22, 1942.

EFFECTS OF SULFONAMIDE THERAPY

- ² Jackson, H. C., and Collier, F. A.: The Use of Sulfanilamide in the Peritoneum. *J. A. M. A.*, 118, 194, 1942.
- ³ Laird, G. J., and Stavern, H.: Intraperitoneal Use of the Sulfonamides. *Cal. and Western Med.*, 56, 293, 1942.
- ⁴ Ravdin, I. S., Rhoads, J. E., and Lockwood, J. S.: The Use of Sulfanilamide in the Treatment of Peritonitis Associated with Appendicitis. *ANNALS OF SURGERY*, 111, 53, 1940.
- ⁵ Mueller, R. S., and Thompson, J. E.: The Local Use of Sulfanilamide in the Treatment of Peritoneal Infections. *J. A. M. A.*, 118, 189, 1942.
- ⁶ Bratton, A. C., and Marshall, E. K., Jr.: A New Coupling Component for Sulfanilamide Determinations. *J. Biol. Chem.*, 128, 537, 1939.
- ⁷ Throckmorton, T. D.: The Peritoneal Response to Locally Implanted Crystalline Sulfonamide Compounds. *Surgery*, 12, 906, 1942.

PREVENTION OF SHOCK AND DEATH BY IMMEDIATE APPLICATION OF A PRESSURE DRESSING TO THE SEVERELY FROZEN LIMBS OF DOGS

AN EXPERIMENTAL STUDY

EGBERT H. FELL, M.D., AND RUSSELL HANSELMAN, M.D.

CHICAGO, ILL.

FROM THE SURGICAL SERVICE, PRESBYTERIAN HOSPITAL, CHICAGO, ILL.

THE GLOBAL WAR has produced many problems. The reports from the various fronts and civil life concerning the serious results following burns, freezing, and crush injuries of extremities have challenged many to further study.

Various authors believe that the three injuries, although due to different causes, are followed by similar local and general reactions and, in the severe

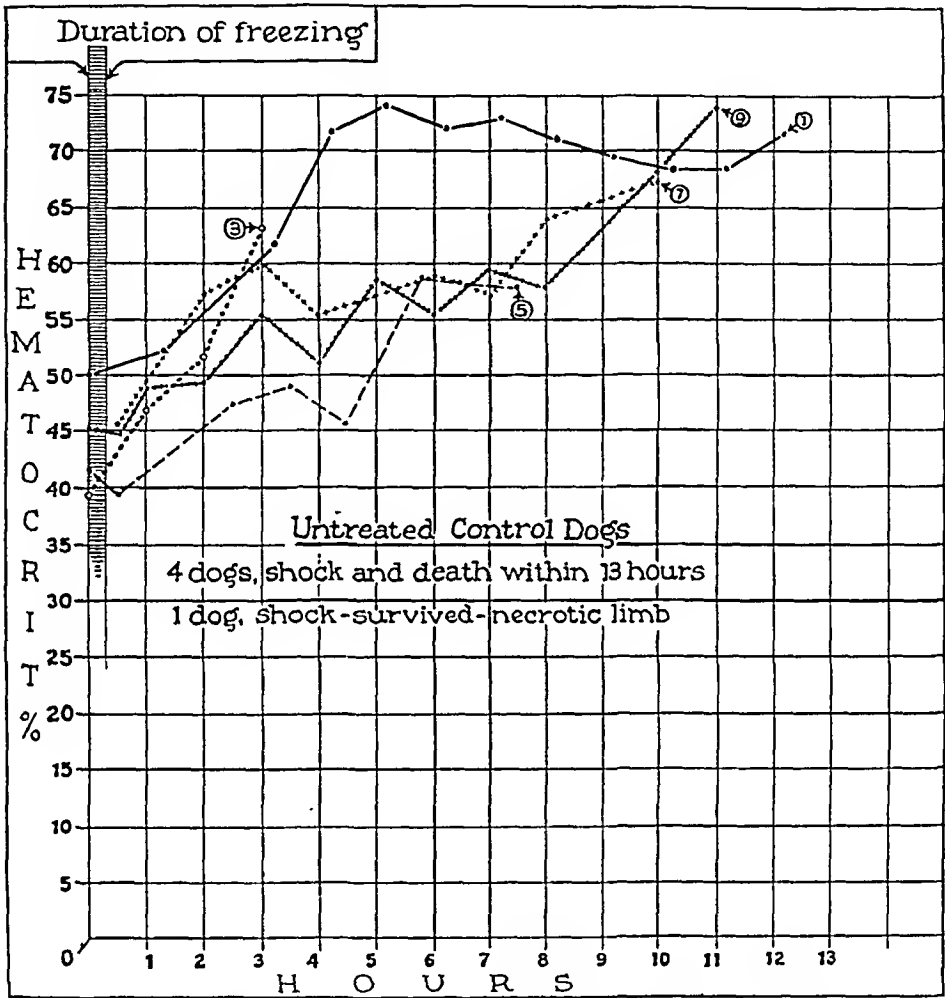


FIG. 1.—Marked swelling of frozen extremity occurred, including the paw.

cases, local swelling soon takes place in a marked degree, often followed by shock and death. This study concerns the prevention of shock and death following a severe freezing injury to an extremity of dogs. Investigators have shown that severe freezing of a dog's extremity is followed by extensive local swelling of the injured part, clinical shock, and death in most cases.

Taking this method of producing these fatal reactions we chose only one form of therapy.

We have been convinced of the importance of pressure dressings for the burned patients and believe, as do Allen¹⁴ and Koch,¹³ that it not only provides a clean, closed wound but minimizes, if properly applied, local swelling, hemoconcentration, and shock, which may result in death. In addition, we wished to study in this experiment the importance of immediate application of a smooth, firmly applied pressure dressing. We have been impressed with



GRAPH 1.—Hematocrit curves of untreated dogs following freezing injury to right hind extremity.

the lack of emphasis placed on the emergency care of the local injured part and the great attention to intravenous and drug therapy. Blalock^{4, 5} has shown that as much as two-thirds of the intravenous plasma administered to dogs with crushed extremities will be lost in or about the injury. Clinically and in the laboratory, shock and death usually follow the local swelling, and much debate has taken place as to whether this is due to local loss of fluids, toxic reaction, both, or a nervous mechanism.

In our experiments, ten dogs were anesthetized with pentobarbital sodium, and maintained under light anesthesia for 10–12 hours. The right hind extremities were immersed to the upper third of the thigh in a mixture

of carbon dioxide snow and 95 per cent alcohol, at -55° C., for 20 minutes. Within two minutes the entire portion was frozen. Five of the dogs received no form of therapy, the legs being allowed to thaw out at room temperature.

To the frozen hind legs of the other five dogs, two to three layers of sheet wadding were applied including the foot and toes, and over this was applied



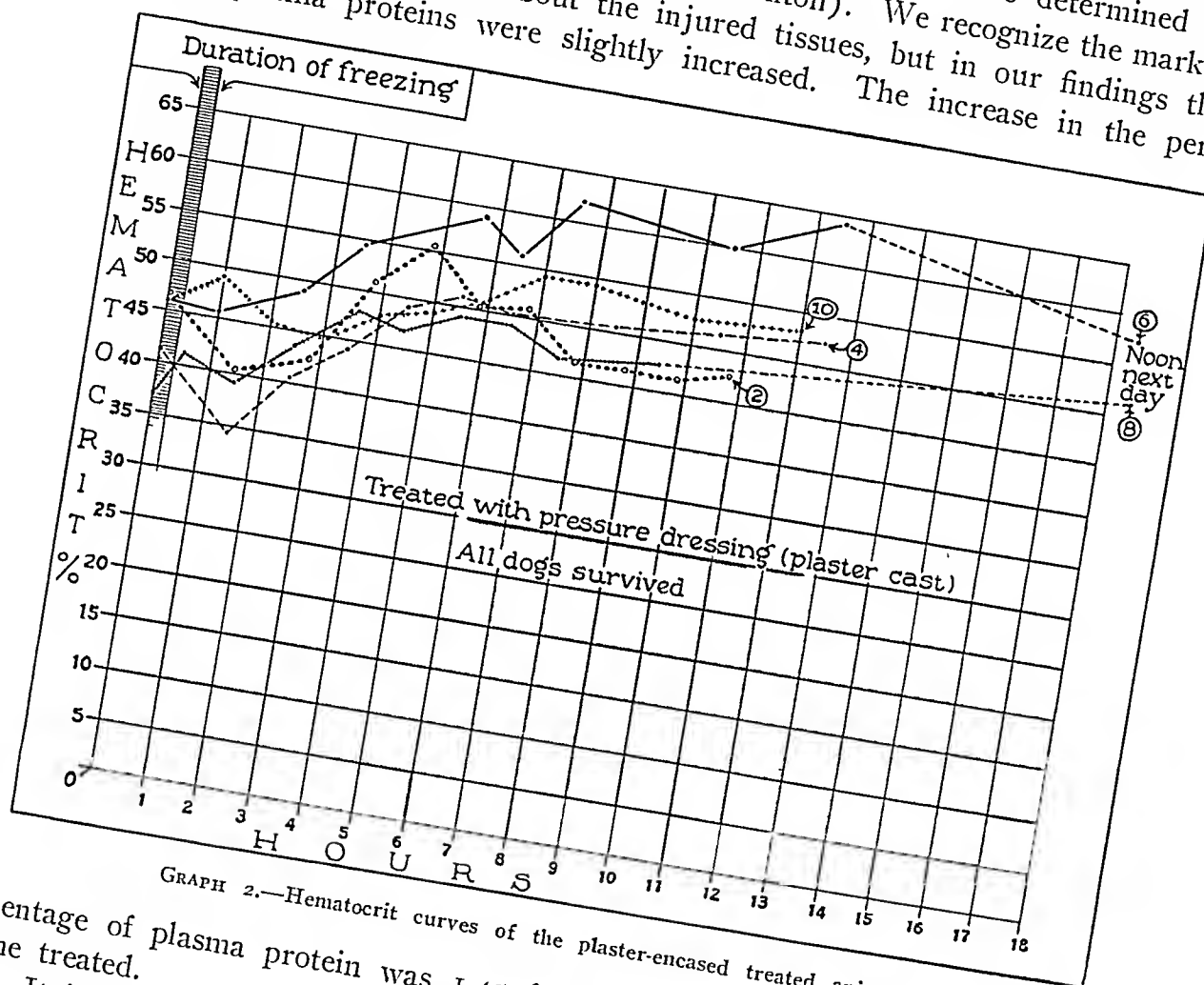
FIG. 2.—Plaster encasement pressure dressing.

smoothly and evenly a plaster encasement. An attempt was made to extend the encasement above the line of frozen tissue.

All five of the untreated dogs developed clinical shock, four of them dying within 13 hours. All of the treated dogs lived, and the maximum increase in the hematocrit was only about one-half as great as in the untreated group. Expressed numerically, the average maximum increase

PRESSURE DRESSING TO FROZEN LEGS

in the hematocrit for the untreated animals was 23.1 points (52 per cent) increase, whereas in the treated group it was only 11.6 points (26 per cent) increase. The rectal temperatures taken directly after freezing showed a decrease of as much as 6° to 7° F. Blood pressures dropped to shock levels in the untreated dogs. Blood was taken at hourly intervals for hematocrit and plasma protein determinations. Plasma proteins were determined by the falling-drop method (Barbour and Hamilton). We recognize the marked loss of plasma into and about the injured tissues, but in our findings the blood plasma proteins were slightly increased. The increase in the per-



GRAPH 2.—Hematocrit curves of the plaster-encased treated animals.

centage of plasma protein was 1.45 for the untreated dogs and 0.56 for the treated.

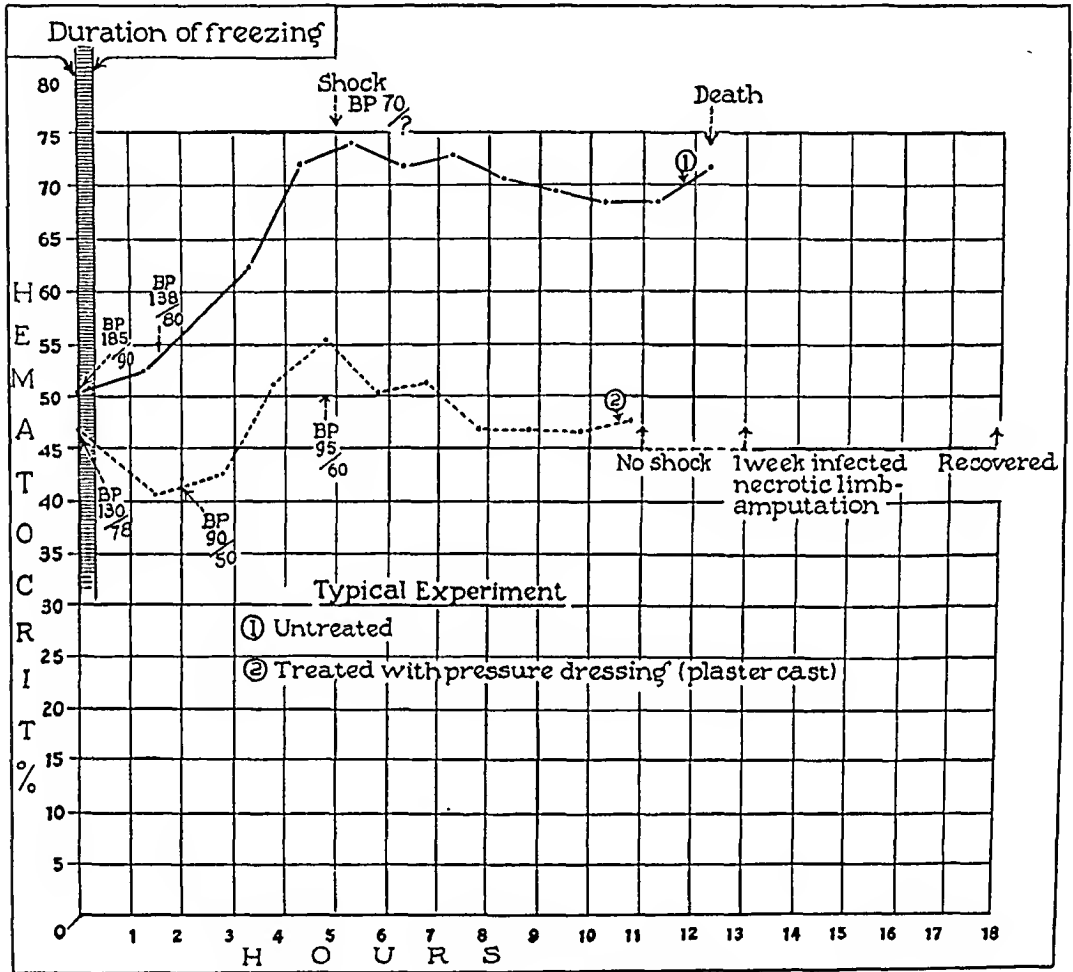
It is of considerable interest, and perhaps of importance, to have seen how slowly the encased legs thawed out; they were cold and moist for 12 hours or longer. We are not sure that the plaster encasement is the preferred method of application of a pressure dressing, but it does afford firm, even pressure splintage and allows for slow thawing.

Four of the five treated dogs developed necrotic limbs. One dog died nine days after freezing and seven days after a hip disarticulation. The cause of death was a generalized purulent peritonitis which may have been secondary to the wound infection. Two dogs had their necrotic infected extremities amputated 8 and 11 days after freezing, and made uneventful

recoveries. The fifth dog had his leg amputated 48 hours after freezing, and likewise recovered.

The plaster encasement of one of the treated dogs became loose, and on the third day it was removed. The leg became necrotic and required a disarticulation. The early removal of the pressure dressing brings up the problem of how long such dressings are necessary.

Sir Thomas Lewis¹ advises in the case of a frozen limb that its arteries



GRAPH 3.—Hematocrit curves of a typical experiment—treated and untreated animal.

may be compressed until thawing is complete and the compressing then be gradually relaxed to allow the blood to return to the limb little by little. There is every reason to believe that limbs less severely frozen than those of our experimental animals can be saved if the compression is uniformly applied to digits and extended above the line of injury just as it is applied to the early burn or wringer injuries.

Further studies are in progress regarding compression, burn, and less severe freezing injuries. Of importance, also, will be the study of compression dressings in cases of partially thawed out or edematous extremities associated with plasma or serum therapy.

PRESSURE DRESSING TO FROZEN LEGS

We have substituted, in two additional cases, an elastic bandage (Acc-type) firmly applied with splintage as a method of pressure dressing, with similar results both as to recovery and hematocrit and plasma protein changes.

It would seem that clinically we could apply the pressure dressings and splintage with advantage to the frozen, compressed, and burned patients. The time for such application is before swelling begins; in other words, immediately when the limb is released from the crushing load, directly after the burn, and before any thawing takes place in the frozen part. This, we believe, is as important as splintage of a fracture at the scene of injury and should be done with the most effective method at hand. Protection of skin and wounds and the prevention of sepsis must not be disregarded.

SUMMARY

The immediate, careful application of pressure dressings, (plaster encasement) prevented shock and death of five dogs whose right hind extremity had been severely frozen. The blood volumes, as determined by the hematocrit, were maintained in this group in levels not producing shock.

REFERENCES

- ¹ Lewis, Sir Thomas: Observations on Some Normal and Injurious Effects of Cold upon the Skin and Underlying Tissues. *Brit. Med. Jour.*, 2, 869-871, December, 1941.
- ² Harkins, Henry N., and Hudson, Jeanne E.: Shock Due to Freezing. *Proc. Soc. Exp. Biol. and Med.*, 32, Part II, 434-435, 1934-35.
- ³ Harkins, Henry N.: Shock Due to Freezing: Shift of Body Fluids and Associated Blood Concentration Changes. *Proc. Soc. Exp. Biol. and Med.*, 32, Part I, 432-435, 1934-35.
- ⁴ Blalock, A.: *Arch. Surg.*, 22, 1610, 1931.
- ⁵ Blalock, Alfred: Effects of Lowering Temperature of an Injured Extremity to which a Tourniquet has been Applied. *Arch. Surg.*, 46, 167, February, 1943.
- ⁶ Duncan, G. W., and Blalock, A.: The Uniform Production of Experimental Shock by Crush Injury: Possible Relationship to Clinical Crush Syndrome. *ANNALS OF SURGERY*, 115, 684, 1942.
- ⁷ Duncan, G. W., and Blalock, A.: Shock Produced by Crush Injury: Effect of Administration of Plasma and Local Application of Cold. *Arch. Surg.*, 45, 183, August, 1942.
- ⁸ Report of Royal Society of Medicine. Effects on Kidney of Limb Compression. *Brit. Med. Jour.*, 2, 884-885, December 2, 1941.
- ⁹ Bywaters, E. G. L.: Crushing Injury. *Brit. Med. Jour.*, 2, 643, November 28, 1942.
- ¹⁰ Bywaters, E. G. L., and Beall, D.: Crush Injuries with Impairment of Renal Function. *Brit. Med. Jour.*, 1, 427, March 22, 1941.
- ¹¹ Beall, D., Bywaters, E. G. L., Belsey, R. H. R., and Miles, J. A. R.: A Case of Crush Injury with Renal Failure. *Brit. Med. Jour.*, 1, 432, March 22, 1941.
- ¹² Mayon-White, R., and Solanet, O. M.: A Case of Limb Compression Ending Fatally in Uremia. *Brit. Med. Jour.*, 1, 434, March 22, 1941.
- ¹³ Koch, S. L.: Panel Discussion: Treatment of Burns. *Bull. A. C. S.*, 27, 106-108, April, 1942.
- ¹⁴ Allen, H. S., and Koch, S. L.: Treatment of Patients with Severe Burns. *S. G. & O.*, 74, 914-924, May, 1942.
- ¹⁵ Muirhead, D. E., Ashworth, C. T., Cregel, L. A., and Hill, J. M.: Experimental Freezing Shock: Changes in Body Fluids and Tissues. *Arch. Surg.*, 45, 863, December, 1942.

THE BLOOD CIRCULATION IN PEDICLE FLAPS*

AN ACCURATE TEST FOR DETERMINING ITS EFFICIENCY

BEVERLY DOUGLAS, M.D., AND RANSOM R. BUCHHOLZ, M.D.

NASHVILLE, TENN.

FROM THE DEPARTMENT OF SURGERY, VANDERBILT UNIVERSITY SCHOOL OF MEDICINE, NASHVILLE, TENN.

WHILE THE NERVE SUPPLY and reorientation of sensation is important in pedicle flaps it does not compare in importance with their blood circulation, an adequate degree of which is vital. A flap can be very useful without sensation but without blood supply its tissues cannot survive for more than a few hours.

Realizing the importance of the problem of blood supply in pedicle flaps which, in the course of reconstructive work, one is frequently called upon to use, we have studied several of the factors which have a bearing on determining the optimum time of transplanting the ends of flaps.

Dr. John Staige Davis defines a pedunculated or pedicle flap as "a mass of tissue, usually the skin and subcutaneous fat, which is raised from its bed but is left attached to the surrounding skin at a selected portion of its periphery." This is the sense in which we shall use the term, except that we should like to qualify it by saying that the pedunculated or pedicle flaps used in most of our experiments have been delayed pedicle flaps, *i.e.*, they have consisted of tubes or ropes of skin usually attached at both but sometimes only at one end, as shown in the accompanying illustrations.

We do not include in this report the special type of pedicle flap which contains a main artery and vein in a narrow pedicle, since in these the circulation is greatly enhanced over that of the ordinary flap in common use in plastic procedures.

On the other hand, we have been careful, as far as possible, in designing flaps to follow the direction of, rather than to cut across the normal course of the arteries and veins, and not to cut across the midline of the body.

It is our impression that the chief factors in the rapid "take" of flaps, by which we mean the ability of the flap tissue to survive the division of the pedicle for purposes of reattachment or shifting, is the development of (1) new vascular connections in the pedicle bed; and (2) progressive development of collateral connections in the direction of the long axis of the flap.

Since in this discussion we shall frequently employ the terms "pedicle skin flap" and "skin graft" we feel it advisable to state the difference in these two useful but very dissimilar forms of transplant. A skin graft is a portion of skin of variable thickness, without fat, which is cut entirely free and placed on a new site from which it must derive its nutrition in order to attach itself, develop its circulation, and survive. A pedicle flap or

* Read before the Nashville Surgical Society, March 13, 1942, Nashville, Tenn.

CIRCULATION IN PEDICLE FLAPS

pedicle skin flap, on the other hand, is a mass of skin and underlying subcutaneous fat which is left attached at some part or parts of its periphery through which part, *viz.*, the pedicle or pedicles, the circulation and nutrition is obtained until the recently shifted pedicle may become attached to its new bed.

It is thus seen that in the skin graft no circulation, except perhaps a plasmatic circulation¹ is present for a considerable time after transplantation, whereas in the flap the tissue remains supplied with blood from one source or another at all times.

It is obvious that the tissue mass of all pedicle flaps (since they contain skin and fat) is much greater than in any skin graft and that they must, therefore, depend for their life upon an adequate blood supply. Unlike a free graft, such masses of tissue would almost never survive free transplantation. This statement is not made in any way to minimize the importance of reestablishment of circulation in the small vessels in the "take" of free grafts of Davis and Traut.² These authors removed small squares of skin and replanted them in their beds. In the first series they rotated the squares 90 degrees and obtained complete takes in 66 per cent, partial takes in 20 per cent and failure in 14 per cent. The second series of squares were rotated 180 per cent with the result that 80 per cent showed complete takes, 20 per cent partial, with no failures. The third, or control series of squares replaced without rotation, took in 100 per cent of the cases.

The work of Goodpasture, Douglas and Anderson¹ corroborates this for human skin grafts on chorio-allantois of chicks by showing a rapid reestablishment of vascular channels from chick membrane to human graft.

While in the case of certain organs, such as the ends of fingers, toes and parts of ears, it is a well known fact that with careful suturing large masses of tissue survive, this is the great exception and is probably due to the accurate matching of parts in a simple terminal system in such a way that arterial and venous flow is rapidly reestablished. For purposes of supplying such masses in reconstructive work, blood supply must be maintained through a pedicle or failure will result.

One of the chief objections to the transfer of tissue by the pedicle flap method has been the delay occasioned by the necessity for leaving the ends of the flap attached to a distant part such as the arm to the face. The splinting required makes such a delay irksome and tedious, not to mention the expense involved.

For a long time in our reconstructive work, we have felt that such flaps were left attached unnecessarily long. No one would intentionally hazard the safety of flap tissue by taking a chance on cutting down the time necessary for an adequate take. On the other hand, we have become more and more convinced that definite tests were possible for determining the adequacy of the circulation at the end of such a flap and that these tests could be relied upon within very close limits of error.

The bearing of the reduction of time and discomfort upon the choice of reconstruction methods as well as upon the economy to all concerned needs no further elaboration.

Recently, one of us succeeded in shifting a flap successfully from the abdomen to the wrist in nine days (Fig. 1). In this patient's case three shifts were accomplished in a total of 35 days, without loss of tissue.



FIG. 1.—Pedicule tube flap, shifted at brief intervals from abdomen to wrist to orbit.

Previous to this, like most workers in this field, we had depended upon clinical reports in making up our minds as to the proper time to shift the pedicles of flaps.

Fomon's text³ gives the opinions of many authors on this point of the earliest safe time at which to shift a flap. One author advises "cutting the pedicle 10-14 days after operation." Another says simply: "Reconstruction by means of tubed flaps are carried out in stages at intervals of three

CIRCULATION IN PEDICLE FLAPS

weeks." Another in speaking of the second stage or cutting the distal pedicle says: "This may be done as soon as collateral circulation has been established in the flap, a process which usually requires three weeks." Another reference speaks of division of the donor pedicle in three weeks and its attachment to the new defect, and, finally, another speaks of the severance of the pedicle still attached to the original donor site in about "three weeks."

We were confirmed in our feeling that flaps are left attached unnecessarily long by the work of German, Finesilver, and Davis.⁴ Briefly, they stated that different authors advised that from several weeks to as many months elapse before dividing one pedicle and making the transfer, but that they felt that while this long delay was never disadvantageous as far as the circulation is concerned it is actually unnecessary. In order to find out how soon the circulation in pedicle tube flaps becomes established after their formation on the abdomen of dogs they used the following methods:

1. They divided one end of the flaps after an intravenous injection of toluidine blue, and as soon as the dye was seen to come through the cut end of the flap, fixed and opened it at the suture line and cleared it for study of the vessels.
 2. Barium in gelatin was injected in the aorta and after the same division roentgenograms were taken to visualize the vessels without opening the flaps.
 3. They studied sections of the flaps in the first series, histologically, by staining with hematoxylin-eosin.
- The flaps in all three series were divided for study after varying periods of time subsequent to their formation.
- They found that flaps immediately removed after their formation showed a few blood-filled vessels crossing at right angles to the long axis of the flap. At 24 hours a few vessels could be seen running almost the entire length of the flaps and, in general, the arrangement of vessels was more definite. At four days this arrangement of vessels was more definite. At seven days the vessels were found to be numerous and to run the entire length of the flap. At 14 days they found very little difference from the findings of the seven-day specimens in the number, character, arrangement, or size of the vessels.

From their experiments these authors conclude that an adequate blood supply in tubed pedicle flaps is established from a single pedicle within seven days, and that the development of this adequate blood supply appeared to be dependent on three factors:

1. An increase in the size of the vessels.
 2. An increase in the number of functioning vessels.
 3. A reorientation of the main vascular channels corresponding to the long axis of the flap.
- It was their feeling that these same facts would hold for human skin

flaps, as they do for those of dogs, and they showed a human case in which the division of a short pedicle flap from the arm to the cheek was begun on the tenth day and completed on the eleventh day, without loss of tissue.

The work of these authors is excellent in quality and gives one an interesting and valuable picture of the rearrangement of blood vessels which takes place in a tubed flap at different stages, but we do not feel that on grounds purely histologic, they are justified in concluding, without actually transferring the ends of their flaps, that a seven-day period is sufficient for the development of a blood supply adequate for the transfer of one end, nor do we feel that their implication that the earliest time for safely beginning the transfer of the ends of tubed skin flaps in humans is probably the seventh or eighth day is necessarily justified on the basis of dog experiments alone. In dogs many factors which influence healing may differ from those in humans. For example, in dogs the normal basal metabolic rate per unit body surface is higher than in humans.

During the past two years we have sought on physiologic grounds to study the development of the circulation in tubed skin flaps in dogs and in humans with a view to the establishment of a test or tests for the accurate quantitative study of circulatory adequacy and, hence, to the determination of an optimum time for transfer of one end of the flap to a new location. Only through such means do we feel that an early transfer can be safely made.

EXPERIMENTAL STUDIES

For convenience our experiments are divided into four types, in all of which the same kinds of tube pedicle flaps were used.

Formation of Flaps.—Dogs weighing between 7 and 12 Kg. were used. The abdomen and anterior and lateral thorax were shaved. Employing nembutal anesthesia, two straight parallel incisions were made longitudinally, which extended approximately from a point three inches from the end of the anterior axillary fold to one or two inches superior to the fold of the groin. The skin and subcutaneous fat down to the superficial fascia were undermined and lifted between these incisions, and the edges of the skin so lifted were approximated with a single layer of sutures to form a tube flap. The ends were left attached to their beds, respectively. The two raw edges of abdominal skin remaining were undermined by spreading scissor points apart at the same depth. They were then approximated by a row of silk sutures in the subcutaneous tissue and another through the skin edges. The tube flaps so formed resembled a suitcase handle and their circumference was one-fourth to one-fifth as great as their length.

SERIES I—BLOOD PRESSURE EXPERIMENTS

The purpose of the several experiments in this series was to determine the systolic blood pressure present in the pedicle of the flaps at different intervals after their formation.

CIRCULATION IN PEDICLE FLAPS

Method: Miniature blood pressure cuffs were employed. The first type consisted of an inflatable tube of thin rubber Penrose drain materials sealed at one end and joined to a rubber connecting tube at the other. This tube was covered with an oiled silk jacket. This cuff was wrapped around the pedicle at one end and joined to a rubber connecting tube at the other. Thus the tourniquet was applied at one end of the flap as one would wrap an ordinary blood pressure cuff on the arm. Over it was bent a small aluminum collar, split at one point to allow the sleeve to come through it. An ordinary mercury manometer calibrated in millimeters was connected to the collar and the usual type of hand pressure bulb was employed to sustain and test pressure. A change in temperature in the flap was used as the criterion for judging the point at which the pressure of the tourniquet was overcome by the systolic blood pressure within the pedicle tested. The apparatus of Brooks,⁵ described in 1925, for measuring temperatures in the extremities was employed. This consists of a thermo-couple mounted in a hypodermic needle and a galvanometer. The temperature change in the pedicle flaps registers very readily, just as is the case in human extremities.

Description of Procedures: With the pressure cuff applied loosely at one end and a firm rubber band to stop all blood flow at the other, the thermocouple needle is introduced into the distal end of the flap and the blood is pressed out of the tube-flap and the air pressure immediately raised to 200 millimeters of mercury (See Fig. 2). The flap is allowed to cool for ten minutes or more and definite readings of the temperature are obtained. The pressure within the tourniquet is then lowered ten millimeters at a time until the temperature in the flap begins again to rise. This point is considered to be the effective systolic blood pressure.

In the case of some of the double pedicled flaps a blood pressure cuff was placed on each end and the two were connected by a "Y" tube to a common manometer creating a system similar to a Lockheed hydraulic automobile brake. By this means simultaneous average pressures could be obtained for the two ends.


Single Pedicled Flaps: In several experiments determinations were made on flaps, one end of which had been left attached after amputation and closure of the other. On some of these the pressures were checked by watching the arterial bleeding stop as the measurable pressure on the tourniquet was increased.

Results: Our findings in these tests are given in the accompanying Table (Fig. 3).

Conclusions.—These findings appear to justify the following conclusions:
1. In double pedicled tube flaps with one end totally occluded the blood pressure registered at the open pedicle gradually increases with the age of the flap. At 48 hours it is about 25 per cent of the normal systolic femoral

BLOOD PRESSURE IN PEDICLE FLAPS

1. Double Pedicled Tube Flaps.

Apparatus	Dog No.	Days after formation	Systolic B.P. m.m. Hg.	B.P. Femoral artery	Diagram of flaps
Single cuff tourniquets.	65	2	25-20		
Other end occluded	65	12	90-80	117	
	65	60	100-90*		
	68	14	60-40		
	39	33	110-100		
	61	42	120	170-165	

* Checked by
division of one
end and watching
cessation of
active bleeding

Double cuff:	65	30	65	
One at each end				
with common	68	14	60-50	
connection to				
manometer				

2. Single Pedicled Flaps.


Single cuff	65	60	110-105	115-117	
Tourniquet	1st Flap		2 days later		
			115	120	
	65	60	100-90	120	
	2nd Flap				

Fig. 3.

CIRCULATION IN PEDICLE FLAPS

pressure, at two weeks it is about 60 per cent, and one month 90 to 95 per cent.

2. Employing tourniquets on both pedicles coupled in a single system, pressure figures are consistently lower on the same dates than the figures for a single tourniquet on a single pedicle. This seems to us to indicate that the pressure within the vessels of the flap must diminish from one end to the other no matter in which direction the blood flows. Consequently

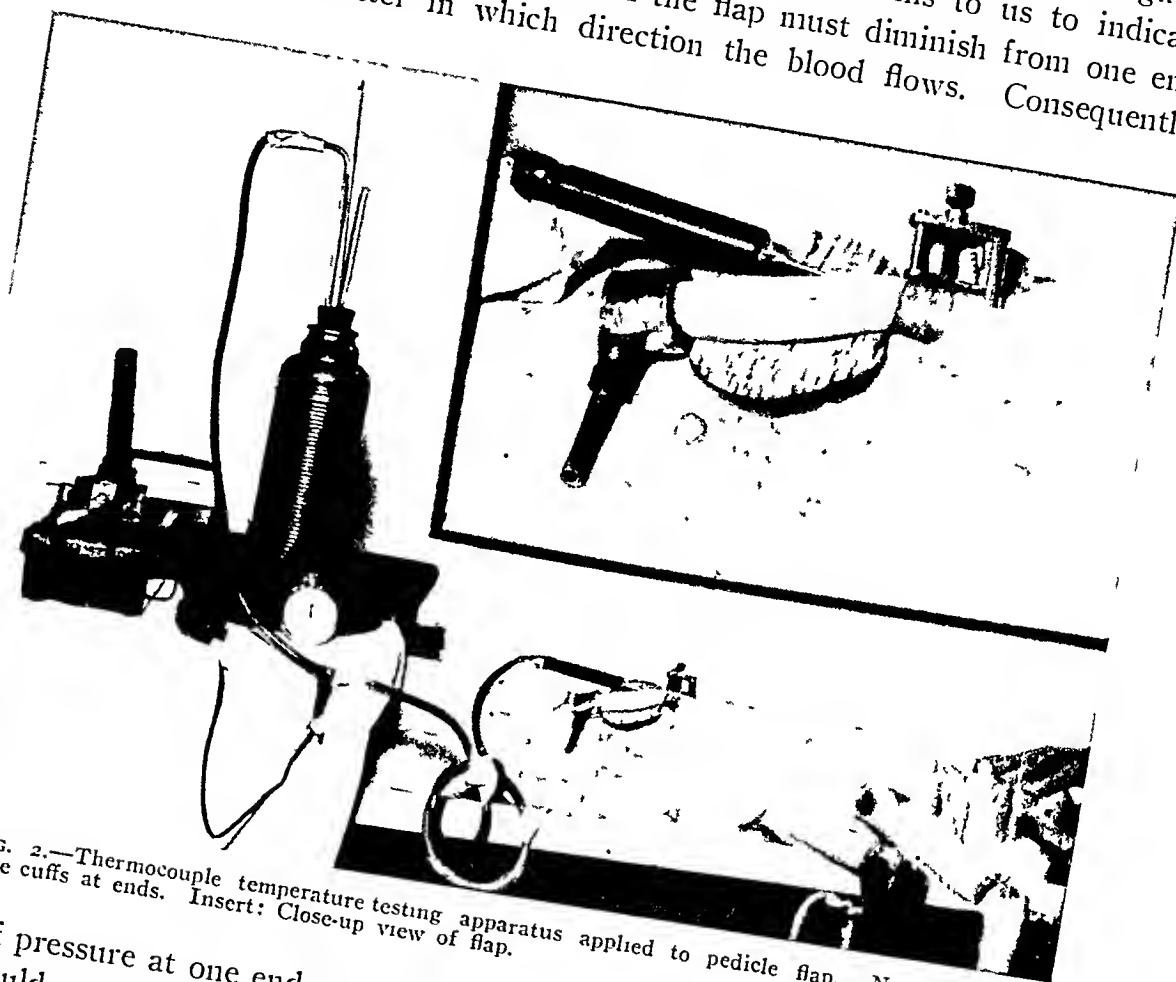


FIG. 2.—Thermocouple temperature testing apparatus applied to pedicle flap. Needle inserted. Pressure cuffs at ends. Insert: Close-up view of flap.

even if pressure at one end was high, *e.g.*, 100 millimeters of mercury, blood flow could not occur on account of back pressure until the tourniquet pressure was reduced to a much lower point at the other end.

3. In single pedicled tube flaps pressures reach 95 per cent of normal-femoral levels after two months.

SERIES II—HAIR GROWTH EXPERIMENTS

It was thought that growth of hair on the flaps might indicate the total effect over a period of days of the primary retardation and gradual re-establishment of circulation in them.

Several flaps were formed in the usual manner after shaving. Their length was roughly three and one-half times their width or three and one-half times the circumference of the tubes. Under a magnifying binocular loupe the lengths of hairs were easily measured at varying intervals following operation. Three levels were chosen for these estimations, the upper, middle

and lower portions of the skin of the flaps and the skin on each side adjacent to that of which the flaps were formed. Ten determinations were made at each site. Results of measurements are shown in Figure 4.

Figures up to six days show only slight differences in the rates of growth

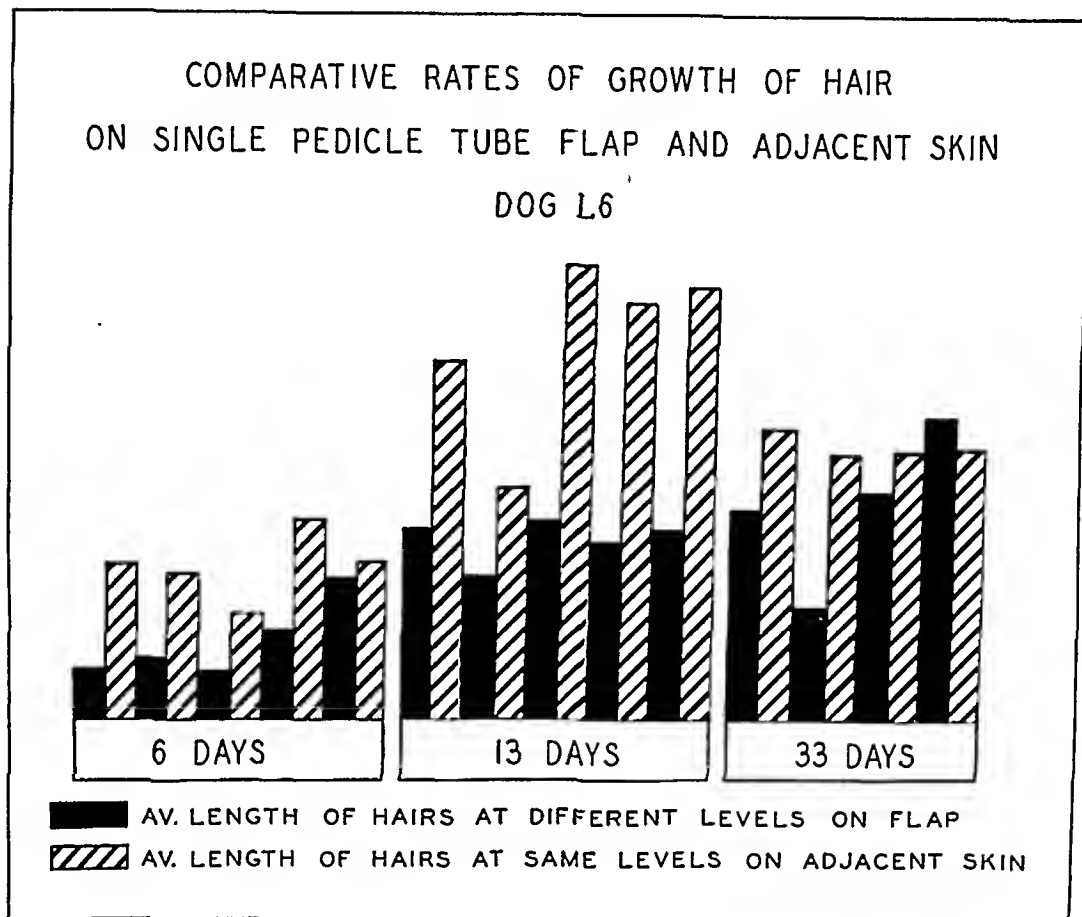


FIG. 4.

on flap and corresponding abdominal skin origin, the edges of which have been undermined and sutured under slight tension.

Dog 61: Determinations on a single pedicle flap formed by division of one end of a double flap (made 23 days before) show that between the seventh and tenth days there are marked differences in growth rates at points on the flap and the corresponding abdominal skin. The hair on the flap is only 68 per cent as long as that on the abdomen.

Dog L. 6: Single pedicle. Lower end attached by strand of tissue. Definite differences after six days. Average length of hair in flap is 72 per cent of that of the adjacent abdominal skin. Also, after 13 days it is 56 per cent and after 33 days it is 78 per cent of that of the adjacent skin.

Conclusions.—From our records we conclude that the growth of hair on double pedicle flaps recently formed is only slightly retarded in comparison with that on adjacent points on the abdominal skin from which the flaps are formed. Likewise, our results on single pedicle tube flaps show that the growth of hair on a blind ended flap is definitely retarded during the first and second six-day periods and that after a month the rate of growth is still somewhat retarded in comparison to that of the hair on the adjacent skin.

CIRCULATION IN PEDICLE FLAPS

SERIES III—TEMPERATURE-RETURN EXPERIMENTS THE TEMPERATURE-RETURN TEST

In these experiments flaps similar to those employed in previous determinations were employed but, in addition, readings were taken on two human pedicle flaps before transfer of one of the ends.

In most cases, without anesthesia, a fixed tourniquet consisting of a band of thin Penrose rubber drain material was wrapped tightly enough around one end to entirely shut off the circulation, then the blood was expressed by compression of the flap between the fingers and a second tourniquet applied at the other end. In a few this expression of blood was omitted. In all thermocouple needle temperatures were taken in the abdominal subcutaneous tissue and in the flap before tourniquets were applied and the needle point was left in the subcutaneous tissue of the flap for subsequent temperature readings, which were made at one minute intervals. After a cooling period, which lasted from 10–15 minutes, the tourniquet at the end away from the needle point was released and the return of temperature recorded over periods varying between 5 and 15 minutes, depending upon the indications. Ordinarily there is a slight initial temperature rise before application of the tourniquet, probably due to a vasodilatation caused by the insertion of the needle, followed by a fall in temperature of from three to six degrees, depending upon the dog's temperature and that of the room. The extent and rate of the rise in temperature which occurs when the tourniquet is removed from either end with the needle in the center or the other end of the flap is taken to indicate the efficiency of the circulation through the flap. A thin cork-guard between the dog's body and the flap prevent the flap from being heated from the body. A pneumatic cuff tourniquet was used in some of these flaps and on others two sharpened fine steel wires transfixed the end of the flap at right angles to each other, so that the vessels of any quadrant or quadrants of the flap could be closed by crossing and making traction on the wires. In all, about 30 experiments were carried out in this series, of which a few of the more typical examples will be discussed in detail. Two of the determinations were on human flaps (See Series IV).

Dog. 28: Figure 5 gives one an accurate picture of the return of the normal temperature in a flap which was formed two weeks before this determination. It is seen that after an initial rise of about 1° C. a fall of 4.1° C. occurred when both ends were completely occluded for ten minutes. On release of one tourniquet the temperature rises to normal in about six minutes showing an excellent circulation to be present at two weeks.

Dog 67: Figure 6 shows resulting graphs of temperature test on pedicle flaps that have been formed for three and seven days, respectively. In the three-day-old pedicle the latent period in the rise of temperature curve and the delayed ascent of the curve are indicative of inadequate blood flow in the flap for the maintenance of viability. However, in the pedicle that has been formed seven days there is an immediate rise in temperature after removal of the tourniquet.

Dog 61 (Figure 7): In this experiment a 107-days-old flap was transfixed at one end by five sharp pointed wires dividing it into quadrants. When blood was allowed through one quadrant no rise occurred. When two quadrants, or one-half of the flap was open, a slow rise occurred, viz., about 0.6° C. in five minutes, whereas the rate increased markedly when all pressure was removed.

Dog 10 (Figure 8): In this and other experiments a series of determinations were made on a single flap as it aged at one hour, three and one-half hours, 72 hours, and six days. There is a lag in the return of circulation through the lower end until the sixth day, at which time it is excellent.

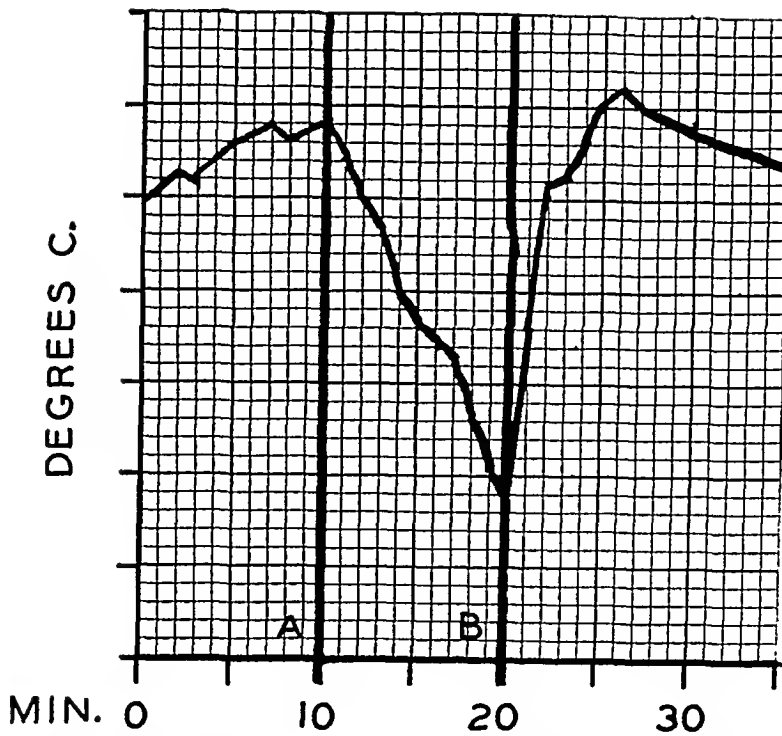


FIG. 5.—Normal temperature curve on pedicle flap. Dog 28—2 weeks postoperative. A—Both tourniquets on. B—Both tourniquets off.

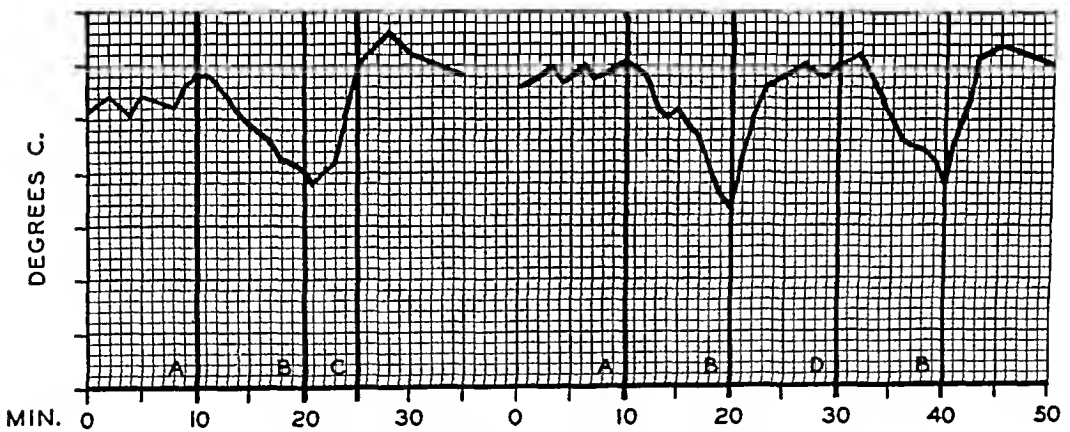


FIG. 6.—Temperature curves on pedicle flap.

Dog 67—Three days postoperative.
A—Both tourniquets on.
B—Lower tourniquet off.
C—Upper tourniquet off.

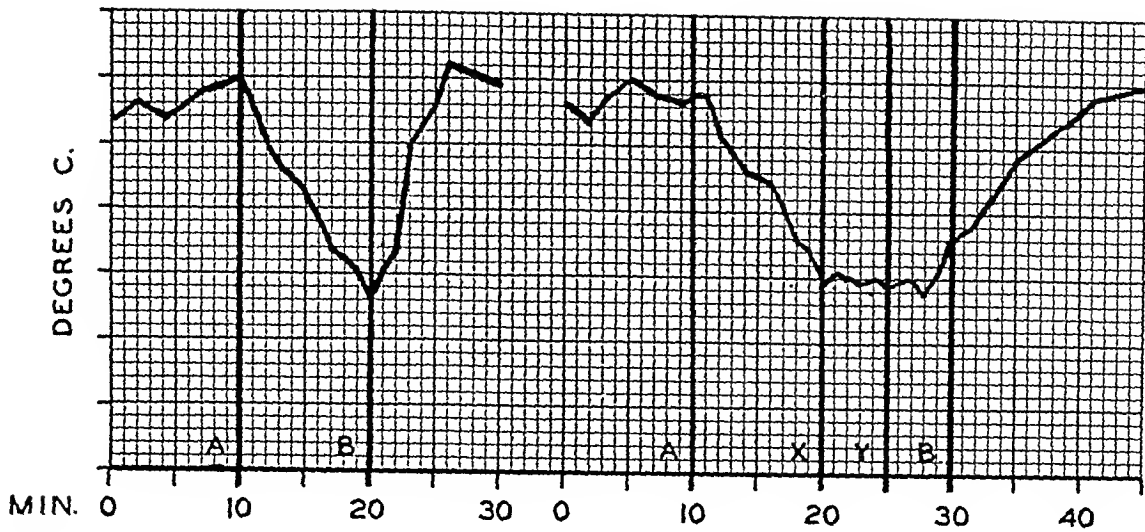
Dog 67—Seven days postoperative.
A—Upper tourniquet on.
B—Upper tourniquet off.
D—Lower tourniquet on.
E—Lower tourniquet off.

Conclusions.—1. Employing the Brooks' thermocouple technic to pedicle flaps normal temperature return curves were established for pedicle flaps which had been formed for periods of time over two weeks.

2. Flaps tested earlier show a progressive increase in circulatory efficiency. Sluggish at one hour, it is slightly better at three and one-half hours, and by the sixth to the seventh day is excellent.

3. Infection seems to retard the return of temperature. This subject needs further study.

CIRCULATION IN PEDICLE FLAPS



..

Fig. 7.—Temperature curves on pedicle flap.

Dog 61—Normal curve.
A—Tourniquet on.
B—Tourniquet off.

Dog 61—Selective circulation by quadrants.
A—Tourniquet on.
X—One-quarter pedicle open.
Y—One-half pedicle open.
B—Tourniquet off.

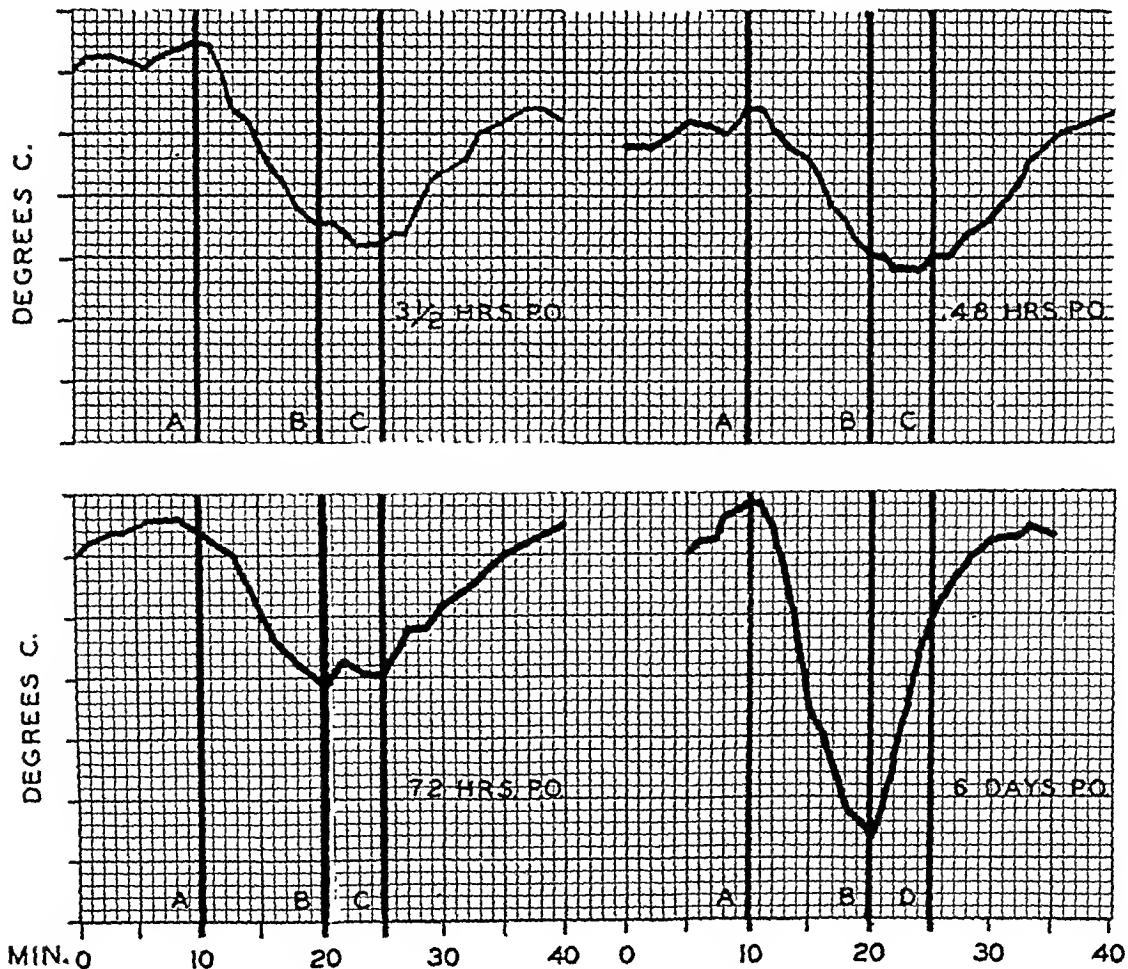


Fig. 8.—Temperature curves on pedicle flap at various postoperative intervals.

A—Both tourniquets on.
B—Lower tourniquet off.
C—Upper tourniquet off.

A—Both tourniquets on.
B—Lower tourniquet off.
D—Both tourniquets off.

4. When a special tourniquet is applied to a flap by quadrants of the tube the efficiency of the circulation appears to be affected in direct ratio to the number of quadrants occluded.

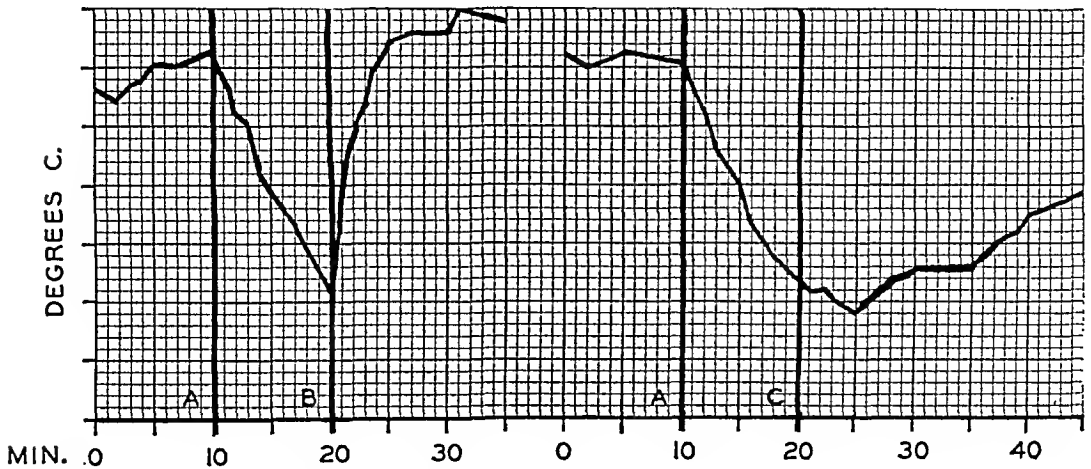


FIG. 9.—Temperature curves on pedicle flap. A—Both tourniquets on. B—Upper tourniquet off. A—Both tourniquets on. C—Lower tourniquet off.

SERIES IV—EXPERIMENTS ON SURVIVAL AFTER TRANSPLANTATION AT VARYING TIME INTERVALS

The purpose of this series of experiments was to determine the earliest safe times after formation of pedicle flaps, in dogs and humans, at which first one end and then the other may be shifted to other sites without jeopardizing the complete viability of the flap. Obviously, in general, the greater the lengths of the flaps in proportion to their widths the less safely can transfers be made, but since all of our flaps were three to five times as long as broad there is little variation in this respect.

We feel that it is fundamentally important to find out in how short a time a whole flap, *i.e.*, both ends may be safely shifted in two stages, one end at a stage, since during this procedure not only must the vessels derive new vascular connections at both ends but the pressure must be sufficient to establish a circulation throughout the entire length of the flap while it is entirely "parasitic," if we may use this word in a topographic or locational sense only. Although this series is not yet completed several studies have already been made of which the following are typical:

Dog 67: Pedicle flap of abdomen had been formed for ten months. Circulation in one end tested with thermocouple needle and found to be good (Fig. 9). Five days later, when temperature curve showed sluggish circulation through the transplanted end, the opposite end was transplanted. The latter end became gangrenous and pulled away from its attachment four days after the second operation.

Dog 14: This dog had had his flap made a year before. After testing, one end was replanted or shifted on 1-26-42. A test on 2-2-42, or nine days after the former shift, showed adequate circulation through the transplanted end. The opposite end was next shifted. Except for a small spot of ulceration at the outer angle of the suture line and a superficial one on the outer surface of the flap, both of which were negligible, the entire flap survived. A test seven days later showed very adequate circulation through both ends.

CIRCULATION IN PEDICLE FLAPS

Human Determinations.—Three humans upon whom pedicle flaps were made during facial reconstructions had the circulation in their flaps studied.

Case No. 1.—J. B., male, age 12. Exenteration of orbit, 1-6-40, for cavernous hemangioma of conjunctiva. Repair of the granulating wound of the orbit was effected by a tube pedicle flap which was first lifted from the abdomen then sutured to the wrist after nine days and, in turn, to the orbital wound edges. Following severance of the distal pedicle, 12 days later a tube of skin and subcutaneous tissue remained attached to the wrist (see Fig. 1).

Several blood pressure determinations were made between the date of severance of the distal pedicle, 2-29-40 and the date of the excision of the flap. These were made by an inflatable ring-cuff slipped over the tube and a water-jacket over its distal end to register volume changes.

Results: 3-14-40 systolic B.P. 30-25 mm. mercury

4- 2-40 systolic B.P. 28-25 mm. (3 readings)

5- 7-40 systolic B.P. 55-25 mm. (3 readings)

5-7-40 systolic blood pressure determined at brachial, 105/98.

Case No. 2.—J. T., male, age 36. During the course of reconstruction of the right cheek and right angle of the mouth a tube was formed from the shoulder to the right cervical region. The return of temperature was tested by the thermocouple needle on 3-20-41, 20 days after the previous shift. It was thought best not to apply tourniquet very tightly. The temperature did not fall markedly, and the rise in temperature afterward, of 25 per cent, was not very significant. The outer end of the flap was shifted the next day and the flap remained entirely viable.

Case No. 3.—L. McD., female, age 19. In course of reconstruction of a portion of the lip and nostril a tube flap of abdominal skin was left attached between these two parts. Determinations of the return of temperature when the tourniquet was released from each end in turn were made on the twenty-fourth day after the nasal end was attached (Fig. 10). These showed a good circulation through both pedicles (Fig. 11). Accordingly the lip end was divided and reimplanted on the cheek the next day. Healing in the new area was uneventful with complete survival.

- Conclusions.*—1. A single pedicled tube flap on the wrist of a boy, age 12, whose brachial blood pressure was 105/98, showed a pressure of 30 after two weeks, 28 after a month, and 55 after two months.
2. In two adult patients upon whose double pedicle flaps temperature-return curves were made by the thermocouple method, the circulation was demonstrated to be adequate, and actual transfer proved this to be the case since both healed without tissue loss.
3. In a boy, aged 12, three shifts of tissue in a tube flap were made in a total of 35 days, an average of 11.2 days per stage.
4. Transplantation in five days of the opposite end of a flap, the pedicle of which, by thermocouple temperature, showed an inadequate circulation, resulted in gangrene and detachment.
5. Transplantation after seven days of the end of a flap, the pedicle of which, by thermocouple temperature test, showed an adequate circulation proved successful. Both ends of the flap showed adequate tests after seven days.



FIG. 10.—Efficiency of circulation through each pedicle of human flap determined by "temperature-return test." Needle inserted; tourniquets applied.

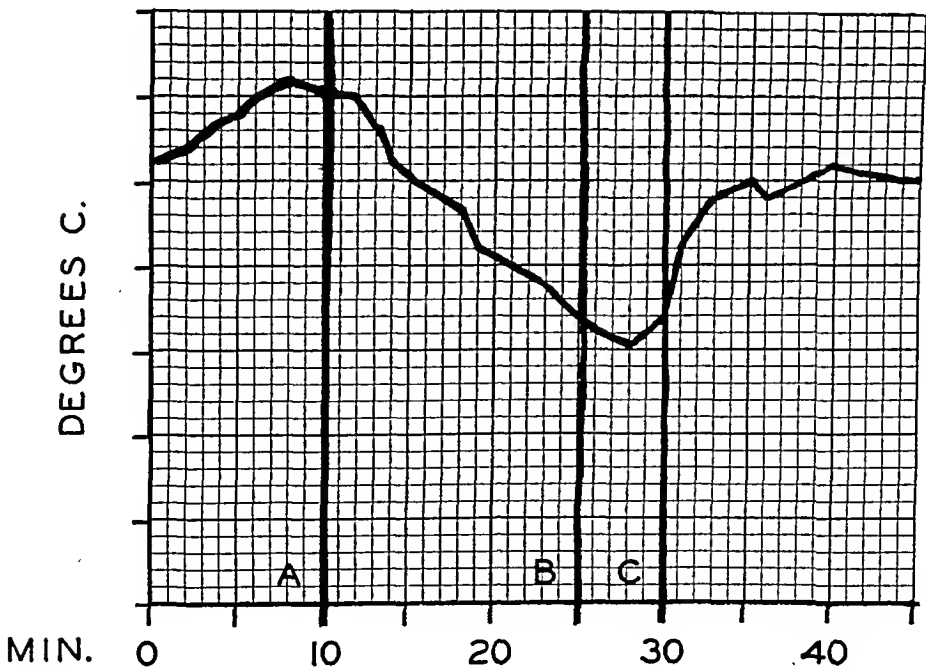


FIG. 11.—Temperature curve on human pedicle flap. Patient L. M. 24 days post-operative. A—Both tourniquets on. B—Lip end off. C—Nose end off.

CIRCULATION IN PEDICLE FLAPS

SUMMARY OF RESULTS

The efficiency of the circulation of double and single pedicle tube flaps in dogs, by which is meant the ability of the vessels to function in such a way as to maintain tissue viability at the other end, was studied by means of four physiologic or functional tests, *i.e.*: (1) Measurement of blood pressure; (2) growth of hair; (3) rate of return of temperature after constriction; and (4) viability or ability to survive after surgical transfer.

1. By employing specially designed miniature cuffs and thermocouple needles in the flaps, their pressures were measured and found to increase with the time interval after their formation, until, at two months, they were 90 to 95 per cent of normal femoral pressure. In a single-ended pedicled human flap the pressure reached 50 per cent normal brachial blood pressure in two months.

2. Hair growth was found to be moderately retarded for 12 days on pedicle flaps in comparison to the growth on the adjacent skin.

3. The rate of temperature return following release of a tourniquet, constriction of which had caused cooling of a flap, was found to be inversely in ratio to the proportion of the pedicle constricted at the end of the flap. This rate was also slow, one hour after the flap was formed, and gradually increased until it almost reached a maximum at six days.

4. Using this temperature return test as a criterion of the adequacy of circulation through the entire flap, the actual ability of several flaps to withstand transplantation was tested by surgically transferring their ends, and practical correlations were obtained between the test and result of transfer both on dogs and on humans.

DISCUSSION.—On anatomic grounds, German, Finesilver and Davis⁴ concluded that the blood vessels in pedicle flaps in dogs was well developed in seven days, running from one end of the flap to the other, and that from that time through the fourteenth day there was little change in the number, character or size of the vessels. None of their pedicle flaps on dogs was shifted to see whether its vessels were actually sufficient to support the life of the flap. Davis and Traut,² in 1925, also showed that the orientation of vessels was important even in small skin grafts.

While agreeing, in general, with their conclusions we felt that physiologic criteria are better than anatomic ones in determining circulatory efficiency. Hence, our work with flaps, along functional lines, has led to development of definite tests.

We would urge any surgeon to exercise caution in judging the circulation of pedicle flaps so as not to transplant the ends too soon. It is wise, of course, not to hazard the life of flap tissue by too great haste. Nevertheless, we feel that with the means which we have established of accurately judging the circulatory condition on each individual and from either end of a flap, much valuable time and expense may be saved and much discomfort safely avoided for the patient. In war time this is of especial importance.

To give an example in the very first tested case (a boy, age 12), we have been able to transfer skin from the abdomen *via* the wrist to the orbit in a total of 35 days, an average of $11\frac{2}{3}$ days per stage. One of the intervals was nine days. In none was partial division of the pedicle practiced, as advocated by German, and his coworkers. If we followed ordinary textbook rules, this transfer would have taken 55 to 63 days, at the very minimum. By following indications of the findings afforded us by the "temperature-return test" as we call it, we have been able to transfer successfully, on a dog, an entire flap of skin eight inches long, so that both ends were reattached in new beds in a period of nine days. More recently, we have succeeded in transferring



FIG. 12.—Rapid transfer of tissue in pedicle flap on dog. Upper end shifted seven days after transplanting lower end. Thermocouple test showed adequate circulation before each shift. No loss of flap tissue occurred.

a flap one and three-fourths by seven inches, on a dog, from one location to another, the two ends being shifted seven days apart, without the slightest ulceration or tissue loss (Fig. 12).

In these two experiments, before transfer of the ends, the "temperature-return test" showed an adequate flow of blood. It is interesting to note that these flaps must be thought of as "autoparasites" since all of their tissue was completely shifted in such short times. Since the vessels in the second were obviously connected, and the blood flowing freely from one end to another in the brief period of seven days, it is probable that the vessels connected up before the process of fibroplasia of the tissues was complete. It

CIRCULATION IN PEDICLE FLAPS

is, therefore, probable at least that the entire flap, although fully alive, could have been pulled away from the dog's abdomen with very little force. Failure resulted in the case of another flap in which an attempt was made to transfer the second end five days after the first when the "temperature-return test" had indicated the circulation to be inadequate.

The earliest time established in dogs for successful transfer of a second end of a pedicle flap after transfer of the first is thus shown to be seven days, and somewhat longer in humans. With more experiments and material we hope through "temperature-return test" to reduce this to a definite point for both.

CONCLUSIONS

1. New methods are described for determining the systolic blood pressure in double and single pedicled tube flaps of skin and subcutaneous tissue.
2. Blood pressures were found to be low shortly after formation of the flaps and gradually to increase with the passage of time until at two weeks they approached normal systolic brachial pressures.
3. The growth of hair is moderately retarded on pedicle flaps up to three weeks after their formation which seems to indicate a temporary slight disturbance of the circulation.
4. Applying the Brooks' thermocouple apparatus a test called the "temperature-return test" has been developed for determining the efficiency of circulation in tubed flaps which indicates an increasing circulatory efficiency from the time of the formation of the flap until the sixth or seventh day in dogs, at which time the circulation through either pedicle to the other end appears to reach almost a maximum efficiency. At this time safe transfer of a pedicle may be accomplished.
5. In dogs and humans, curves indicating the efficiency of blood circulation in flaps have been correlated with the ability of the flap to completely survive surgical transplantation.
6. Evidence accumulated from a number of human cases appears to indicate the advantages of this physiologic test in individualizing the circulatory efficiency of the flap so as to save time, with safety, between stages, and to avoid discomfort for the patient incident to well meant but unnecessary delays. In war surgery the importance of this point is obvious.
7. The magnitude of the time-saving is to be determined as further cases accumulate.

REFERENCES

- ¹ Goodpasture, E. W., Douglas, B., and Anderson, K.: A Study of Human Skin Grafted Upon the Chorio-Allantosis of Chick Embryos. *Jour. Exp. Med.*, 68, 891, 1938.
- ² Davis, J. S., and Traut, H. F.: Origin and Development of Blood Supply of Whole Thickness Grafts. *ANNALS OF SURGERY*, 82, 871, 1925.
- ³ Fomon, S. S.: Williams and Wilkins Co., Baltimore, 1939, pp. 230-231.
- ⁴ German, W., Finesilver, E. M., and Davis, J. S.: *Arch. Surg.*, 28, 27, 1933.
- ⁵ Brooks, Barney: New Methods for Study of Diseases of the Circulation of Extremities. *Jour. Bone & Joint Surg.*, 7, 316, 1925.

PERFORATED PEPTIC ULCER*

FRANCIS X. TIMONEY, M.D.

NEW YORK, N. Y.

FROM ST. VINCENT'S HOSPITAL, FIRST AND SECOND SURGICAL DIVISIONS, GEORGE R. STUART, DIRECTOR, 1ST SURGICAL DIVISION; RAYMOND P. SULLIVAN, M.D., DIRECTOR, 2ND SURGICAL DIVISION; NEW YORK, N. Y.

THE SUBJECT of perforated peptic ulcer merits discussion. The condition is prevalent in hospitals that have busy emergency services, of which St. Vincent's Hospital is an example. The high mortality reported by various authors throughout the country attest to the seriousness of this condition. Because of this, the cases occurring at St. Vincent's Hospital within the past eight years have been studied. Most of these cases have been operated upon by the younger members of the Attending Staff and by House and Resident Surgeons under their supervision. Two hundred fifty-four cases have been studied. In studying the charts of these patients observations of interest were made. Four patients perforated on the ward while undergoing medical treatment for ulcer. Another patient perforated in a physician's office while undergoing a gastric lavage. Several perforated while carrying a heavy load or doing strenuous work. This is in accordance with observations made by McCreery.⁹ Others perforated while drinking beer or highballs.

The accuracy of the clinical diagnosis of perforated peptic ulcer is high, as shown by the following statement: Diagnosis: Correct in 238 operated cases; incorrect in eight operated cases; incorrect in two cases, proved by autopsy.

The following is a list of the incorrectly diagnosed cases:

1. Bleeding ulcer—autopsy showed unrecognized peritonitis due to ruptured ulcer.
2. Acute appendicitis.
3. Acute appendicitis.
4. Acute appendicitis.
5. Acute appendicitis.
6. Acute appendicitis—died 12 days postoperatively of hemorrhage from ulcer which had ruptured.
7. Acute hemorrhagic pancreatitis—no operation performed due to extreme secondary shock. Autopsy revealed generalized peritonitis due to ruptured duodenal ulcer.
8. Acute cholecystitis—At operation, chronically inflamed gallbladder was removed and perforated ulcer repaired.
9. Strangulated hernia.
10. Patient perforated twice, and gastric perforation was repaired each time. At time of second perforation, biopsy from ulcer showed inflammatory

* Read before the New York Academy of Medicine, Surgical Section, November 6, 1942.

PERFORATED PEPTIC ULCER

tissue. One year after second operation, patient was readmitted to hospital with gastric hemorrhage. Died soon after. Autopsy revealed gastric cancer. We believe that ulcer was carcinomatous from the beginning.

Percentage of error—4.2 per cent. Diagnosis was correct in 238 out of a total of 248 cases, either operated upon or proven by autopsy. The percentage of error is only 4.2 per cent. This high degree of accuracy in clinical diagnosis is attributable to the fact that this type of case is seen regularly by members of the Attending and Resident Staffs. Also, many of the surgeons are on the Staffs of other city hospitals, with busy emergency services, thereby widening their experience with this condition.

One hundred twenty-six cases were described as perforated gastric ulcers; 116 as duodenal ulcers; and two as marginal ulcers. At times, difficulty was experienced by the operator in determining the site of the ulcer. Several were diagnosed as perforated gastric ulcers, only to have autopsy reveal the location as duodenal. The opposite has also held true, where a surgeon of wide experience diagnosed a "large duodenal perforation" only to have autopsy reveal that the perforation was gastric.

Sex Incidence.—The disease is seen predominately in men—male, 246 cases; female, 8 cases. Roentgenologic examinations for air or gas under the diaphragm have been of limited value in the cases studied: Positive for air under diaphragm 93 cases; negative for air under diaphragm 83 cases; total of 176 cases.

By history and physical examination, experienced clinicians diagnose perforated ulcers more accurately than by roentgenologic examination. The routine taking of roentgenograms, that will delay operation in cases already diagnosed clinically, might better be abolished.¹⁰ We believe roentgenologic studies to be of most value in the occasional case where the clinical picture is not definite.

Mortality.—The following table shows our total and operative mortality:

TABLE I	
Total number of cases.....	254
Total mortality.....	48
Total operated upon.....	246
Operative mortality.....	19.5%

This mortality compares favorably with that reported in recent years from various sections of this country and England, which averages around 20 per cent (See table II).

The notable exception is that of Graham,⁷ who reports the strikingly low mortality of only one death in 51 operated cases. This is all the more remarkable because his report covered the years 1929 to 1935, a period when Wangensteen suction was not generally used, and only at the end of this period was sulfanilamide first brought to our attention. Graham graciously acknowledges the early correct diagnosis and the speed with which the family physicians of Toronto referred the patients to the hospital.

TABLE II
MORTALITY STATISTICS

Author	Total Cases	Mortality
Berson, H. L.	151	15.2%
Davidson, T. C., and Rudder, F. F.	155	28%
DeBakey, M., and Odum, C. B.	211	17 3%
Donald, D. C., and Barkett, S. M.	116	18.5%
Eliason, E. L., and Thigpen, G. M.	70	21.43%
Fallis, L. S.	100	20%
Years 1917-26—62 5%		
Years 1926-36—11 9%		
Graham, R. R.	51	1.96%
McCreery, J. A.	170	20 5%
Martz, H., and Foote, M. II.	50	26%
Parker, E. F.	52	27%
Marshall, S. F., and Keicher, P. C.	46	13%
O'Donoghue, J. B., and Jacobs, M. B.	200	24.5%
Read, J. C.	100	30%
Ross, A., and Letourneau, C.	220	17.7%
Ross, J. C.	175	16%
Sangster, A. II.	100	23%
Thompson, H. L.	424	28.7%

Nevertheless, Graham sets an example which all should strive to follow. Due to the activity of the ambulance service most patients were brought *early* to hospital.

The tables of total cases and duration of symptoms follow:

HOURS -				
To 6 Hours	6-12 Hours	12-24 Hours	Over 24 Hours	Not Stated
158	50	15	17	14
62 2%	19 6%	5.9%	6.6%	
Total cases stated.....				240
Duration of symptoms not stated				14
Total.....				254

DURATION OF SYMPTOMS IN 48 FATAL CASES				
Under 6 Hours	6-12 Hours	12-24 Hours	Over 24 Hours	Not Stated
17	11	6	6	8
10.8%	22.4%	40%	35%	

We have tried to present the general picture of perforated peptic ulcer as occurring during the past eight years. With the advent of intraperitoneal use of sulfanilamide, we noted improvement and better results in our cases. Our Staff has not changed materially during the last eight years. We felt that the improvement noted in our results might possibly be due to increased knowledge, experience, and technical skill on the part of the Attending Staff. Accordingly, the last 50 consecutive cases, before those in which sulfanilamide has been used, were analysed. These are compared with those in which sulfanilamide was used in the peritoneal cavity. The following tables show the results:

PERFORATED PEPTIC ULCER

TREATED PEPTIC ULCER							
AGES OF 50 RECENT CASES, WITHOUT INTRAPERITONEAL USE OF SULFANILAMIDE							
YEARS		YEARS		YEARS			
10-20	2	20-30	6	30-40	11	40-50	14
16%		12.2%		22.4%		28.5%	
AGES OF 49 CASES WITH INTRAPERITONEAL USE OF SULFANILAMIDE							
YEARS		YEARS		YEARS			
10-20	2	20-30	6	30-40	11	40-50	14
4.08%		12.2%		22.4%		28.5%	
DURATION OF SYMPTOMS OF 50 RECENT CASES WITHOUT INTRAPERITONEAL USE OF SULFANILAMIDE							
HOURS		HOURS		HOURS			
To 6 Hours	32	6-12 Hours	10	12-24 Hours	1	Over 24 Hours	4
64%		20%		2%		8%	
RESULTS OF 50 RECENT CASES TREATED WITHOUT SULFANILAMIDE							
Total cases.....		50		Deaths.....		12	
Recoveries.....		38		Not Stated		3	
DURATION OF SYMPTOMS OF 49 CASES WITH INTRAPERITONEAL USE OF SULFANILAMIDE							
HOURS		HOURS		HOURS			
To 6 Hours	26	6-12 Hours	16	12-24 Hours	2	Over 24 Hours	5
53.06%		32.6%		4.08%		10.2%	

Of these recent 50 cases in which there was no intraperitoneal use of sulfanilamide, 12, or 24 per cent, died. The

Of these recent 50 cases in which there was no intraperitoneal use of sulfanilamide, 12, or 24 per cent, died. The following is a brief résumé of the fatal cases:

RÉSUMÉ OF FATAL CASES NOT TREATED WITH SULFANILAMIDE

1. Male, age 56, eight hours symptoms, died 12 days postoperatively of intestinal hemorrhage. Had appendectomy at operation.
2. Male, age 51, seven hours symptoms, died seven days postoperatively of generalized peritonitis. Had gastro-enterostomy.
3. Male, age 38, two and one-half hours symptoms, died two days postoperatively. Autopsy revealed generalized peritonitis.
4. Male, age 49, four and one-half hours symptoms, died three days postoperatively of pulmonary atelectasis.
5. Male, age 67, four and one-half hours symptoms, died seven days postoperatively of bilateral lobar pneumonia.
6. Male, age 59, nine and one-half hours symptoms, died one day postoperatively of pulmonary atelectasis. In very poor condition on admission. Decision to operate is to be questioned.
7. Male, age 53, four and one-half hours symptoms, died three days postoperatively. Autopsy showed generalized peritonitis and a large gastric ulcer.
8. Male, age 52, five and one-half hours symptoms, died 13 days postoperatively. Course was stormy, had lobar pneumonia. No autopsy.
9. Male, age 50, six hours symptoms, died two days postoperatively. Was on Medical Ward undergoing treatment when perforation occurred. Died of postoperative pneumonia.

10. Male, age 58, three hours symptoms, had advanced peritonitis and died on the operating table. Operator believed that perforation must have occurred before the stated time.

11. Male, age 39, four hours symptoms, died three days postoperatively of delirium tremens.

12. Male, age 29, ten hours symptoms, died five days postoperatively of delirium tremens.

In reviewing these 12 postoperative deaths, we see that infection contributed directly to the fatal outcome, in the four cases of death, by generalized peritonitis, and in the five cases of fatal pulmonary complications. Infection might well have been present in the two fatal cases of delirium tremens. We believe that if there had been a local intraperitoneal use of sulfanilamide in the above stated cases, infection would have been controlled, lessened, or prevented.

Unfortunately, this represents a serious group of cases. Eight patients were 50 years of age or over, and two suffered from chronic alcoholism, and finally succumbed from delirium tremens.

We compare this with 49 cases of perforated peptic ulcer, treated consecutively, with the intraperitoneal use of sulfanilamide. In addition, each patient had a small amount of sulfanilamide placed in the wound.

Cases treated with intraperitoneal use of sulfanilamide: Total number, 49. Deaths, 2. Recoveries, 47.

Résumé of fatal cases treated with intraperitoneal use of sulfanilamide:

1. No. 26317, female, duration of symptoms six hours, age 31. W.B.C. 7100, 52 per cent polys. Findings at operation—perforated gastric ulcer, with marked peritoneal reaction. Procedure: Closure and drainage. Died one day after operation. Autopsy showed generalized peritonitis.

2. No. 28423, male, age 63, admitted to hospital with symptoms of abdominal pain and tenderness in R.L.Q., of six hours duration. W.B.C. 6750, 74 per cent polys. Admission diagnosis was "gastro-enteritis" but "patient should be observed for possible acute appendicitis." Twelve hours later, rigidity developed, and diagnosis of ruptured ulcer was made. He was operated upon more than 18 hours after onset of symptoms. Procedure: Closure and drainage. Died on third postoperative day, with chest signs of postoperative pneumonia. No autopsy obtained. In this case an early diagnosis was missed.

Of these 49 cases treated locally with sulfanilamide, 22 were drained and 27 were not drained. From this, we are unable to draw any conclusion as to the effect of drainage when sulfanilamide is used locally.

In the total 246 cases operated upon, wound infections were noted on the charts in 63 instances, an incidence of 25.6 per cent: Total cases operated upon, 246. Wound infections, 63. Incidence of wound infection 25.6 per cent.

PERFORATED PEPTIC ULCER

In the 49 cases treated with the local use of sulfanilamide, there were four infections, an incidence of 8.1 per cent.

Mueller and Thompson,²⁰ of Roosevelt Hospital, recommend the local use of sulfanilamide when any form of peritonitis is encountered at operation. O'Donoghue and Jacobs¹⁴ recommend the use of sulfanilamide in cases showing bacterial contamination. Griswold and Antonic⁸ report the use of sulfanilamide in the peritoneal cavity, and in the wound, in 12 cases, with one death. They also made blood studies showing that the concentration of sulfanilamide in blood rapidly reached a peak of about six milligrams per 100 cc. of blood, with a gradual disappearance in 24 to 48 hours. We have used 8-12 grams of sterile sulfanilamide powder. The drug is sprinkled at the site of perforation and also the entire area exposed by the incision. In the process of wound closure one or two grams are placed in the abdominal wall.

We believe that several factors besides chemotherapy merit consideration for the improvement noted in our report, *i.e.*, Wangensteen suction and parenteral administration of fluids. It prevents vomiting with lessened strain on the logic rest to the stomach. It prevents gastric distention, with lessening of consequent tension on serosal sutures. We wish to stress the importance of the preoperative use of Wangensteen suction.

As soon as the diagnosis is made at the hospital, Wangensteen suction is begun. This helps to prevent the spilling of gastric contents into the peritoneal cavity because perforation frequently occurs when the stomach is filled. This spilling causes peritonitis. There is usually a period of several hours before operation is performed. This is valuable time lost. The time is consumed in blood studies, roentgenologic studies, preparation of the patient, setting-up of the operating room, and summoning the Attending Surgeon. During this time, continuous Wangensteen suction prevents further spilling into the peritoneal cavity. Likewise, lessened spilling will occur as a result of forceful respiration during the induction stage of general anesthesia.

By means of parenteral therapy of intravenous administration of saline or glucose solution, plasma or whole blood, as indicated, fluid balance and nutrition is better maintained. The incidence and severity of pulmonary complications is materially lessened by the intravenous administration of an appropriate sulfonamide during that period when a sick patient cannot take sufficient by mouth.

SUMMARY.—A total of 254 cases were studied. The clinical diagnosis of perforated peptic ulcer was correct in more than 95 per cent of cases. There were 246 operations performed, with 48 deaths, an operative mortality of 19.5 per cent. This is compared with a series of 49 recent cases in which sulfanilamide was implanted in the peritoneal cavity and in the wound, with two deaths, an operative mortality of four per cent. In a total of 246 operated cases there were 63 instances of wound infection, an

incidence of 25.6 per cent. In the 49 cases treated with intraperitoneal implantation of sulfanilamide there were four wound infections, an incidence of eight per cent. The importance of the preoperative use of Wangensteen suction is emphasized.

CONCLUSIONS

The implantation of powdered sulfanilamide in the peritoneal cavity and in the wound is indicated in the surgical treatment of perforated peptic ulcer. It is an effective agent in reducing mortality and lessening the occurrence of postoperative infection of wounds.

REFERENCES

- ¹ Berson, H. L.: Acute Perforated Peptic Ulcer: An 18-year Survey. *Am. J. Surg.*, 56, 385-394, May, 1942.
- ² Davison, T. C., and Rudder, F. F.: Factors Influencing the Mortality of Perforated Peptic Ulcer. *South. Surgeon*, 9, 75-85, February, 1940.
- ³ DeBakey, M., and Odom, C. B.: Significant Factors in the Prognosis and Mortality of Perforated Peptic Ulcer. *South. Surgeon*, 9, 425-436, June, 1940.
- ⁴ Donald, D. C., and Barkett, S. J.: Acute Perforated Peptic Ulcer Syndrome with Surgical Management. *Am. J. Surg.*, 56, 406-413, May, 1942.
- ⁵ Eliason, E. L., and Thigpen, G. M.: The Effect of Perforation on Peptic Ulcer Results. *Amer. J. Surg.*, 41, 419-426, September, 1938.
- ⁶ Fallis, L. S.: Perforated Peptic Ulcer: An Analysis of 100 Cases. *Amer. J. Surg.*, 41, 427-437, September, 1938.
- ⁷ Graham, R. R.: The Treatment of Perforated Duodenal Ulcers. *Surg. Gynec., and Obst.*, 64, 235-238, February, 1927.
- ⁸ Griswold, R. A., and Antoncic, R. F.: Perforated Peptic Ulcers. *ANNALS OF SURGERY*, 113, 791-798, May, 1941.
- ⁹ McCreery, J. A.: Perforated Gastric and Duodenal Ulcer. *ANNALS OF SURGERY*, 107, 350-358, March, 1938.
- ¹⁰ MacGuire, C. J.: Personal communication.
- ¹¹ Martz, H., and Foote, M. N.: Analysis of 50 Cases of Perforated Peptic Ulcer. *Amer. J. Surg.*, 48, 634-640, June, 1940.
- ¹² Parker, E. F.: The Late Results in Acute Perforated Peptic Ulcer Treated by Simple Suture. *Surgery*, 10, 49-63, July, 1941.
- ¹³ Marshall, S. F., and Keleher, P. G.: Management of Acute Perforation of Peptic Ulcer. *Surg. Clin. N. A.*, 20, 757-766, June, 1940.
- ¹⁴ O'Donoghue, J. B., and Jacobs, M. B.: Acute Perforation of Gastric and Duodenal Ulcer: A Study of 200 Consecutive Operated Cases. *Ill. Med. Jour.*, 81, 62-69, January, 1942.
- ¹⁵ Read, J. G.: Review of 100 Cases of Ruptured Peptic Ulcer. *South. Surg.*, 7, 436-442, October, 1938.
- ¹⁶ Ross, A., and Letourneau, C.: Perforated Peptic Ulcer: Analysis of a Series of 228 Consecutive Cases. *Can. M. A. J.*, 41, 473-479, November, 1939.
- ¹⁷ Ross, J. C.: Perforated Peptic Ulcer; A Review of 175 Personal Cases. *Brit. M. J.*, 2, 665-667, November, 1940.
- ¹⁸ Sangster, A. H.: Perforated Peptic Ulcer: An Analysis of 100 Consecutive Cases. *Lancet*, 2, 1311-1313, December 23, 1939.
- ¹⁹ Thompson, H. L.: Acute Perforation of Peptic Ulcer: Immediate and Late Results in 500 Cases. *J. A. M. A.*, 113, 2015-2019, December 2, 1939.
- ²⁰ Mueller, R. S., and Thompson, J. E.: The Local Use of Sulfanilamide in the Treatment of Peritoneal Infection. *J. A. M. A.*, 118, 189-193, January 17, 1942.

PERFORATED PEPTIC ULCER

DISCUSSION.—Constantine J. MacGuire, M.D., (New York): This review by Dr. Timoney on perforated peptic ulcers is very well justified. In his bibliography he quotes 17 previous reviews in this country and England, and his series of 254 cases is the largest in that group with the exception of that by H. L. Thompson.¹⁹

St. Vincent's Hospital has one of the most active ambulance services in the City, which makes the findings in this paper all the more significant. It is rather striking that through all the reports the mortality percentages correspond rather closely; the largest being between 15 and 30 per cent, with the exception of Roscoe Graham's report on 51 cases with only a two per cent mortality. This is very difficult to understand, and may be explained by the relatively small number of cases. In all reports there is usually a wide group of operators because these cases come in at night as emergencies and are subjected to a rotating list of surgeons, but the main factor seems to be the interval between onset and operation rather than the skill of the individual operator. It is interesting to note that although the lowest mortality was in those operated upon under six hours and next those operated under 12 hours, that those operated upon over 24 hours had a lower mortality than those between 12 and 24 hours.

There has always been a certain amount of dispute as to the site of these ulcers. They are usually in the region of the pylorus, and it is often difficult to determine whether they are prepyloric or postpyloric. Personally, I believe that a rough yard-stick is as follows: Perforation is twice as frequent prepyloric as duodenal, while massive hemorrhage is twice as often duodenal as prepyloric. One hundred seventy-four of these cases had roentgenograms taken before operation, and I think that the fact only 91 were positive for air under the diaphragm would be an indication that roentgenograms can be dispensed with if it is going to be the cause of delay.

Some clinics have advised immediate resection in these cases. I think we all feel that resection should be reserved for those callous ulcers with large perforations, with cheesy walls, which are hard to close. Many of these perforations are very small and easily closed, and the patient recovers by careful and complete follow-up records. I know that Dr. Timoney attempted this, and felt that the percentage of return visits was not large enough to justify conclusions. This, once again, proves what we have all learned so painfully, that for statistical purposes follow-up systems are worthless unless the percentage of returns is over 90 per cent.

Forty-nine cases were treated with sulfanilamide in the peritoneum. Conclusions based on this number of cases must be guarded, but the drop in the mortality percentage is impressive. I feel that it is imperative, where sulfanilamide is used, that drainage is employed, as in certain cases the use of the sulfa drugs excites marked peritoneal exudate, enough to alarm the nurses in attendance. If no drainage is employed this exudate has been known to lead to great distension and paralytic ileus. I am now referring not only to perforated ulcers but to any abdominal case where this drug is employed.

These statistical analyses of a rather common and dramatic surgical emergency are very useful, and I would like to see Dr. Timoney give a subsequent report at the end of another five years.

ATRESIA OF THE DUODENUM

A CASE SUCCESSFULLY TREATED BY DUODENODUODENOSTOMY

CHARLES S. WARD, JR. M.D., AND FREDERICK W. COOPER, JR. M.D.

ATLANTA, GA.

FROM THE DEPARTMENT OF SURGERY, EMORY UNIVERSITY, ATLANTA, GA.

COMPLETE CONGENITAL ATRESIA of a segment of the small intestine is a fatal condition unless the patient is operated upon early. Since the first case of congenital atresia of the duodenum successfully treated by operation was reported by Ernst,¹ in 1916, many reports have appeared in the literature. However, only 14 patients with a complete atresia of the duodenum have survived. For this reason, the following case is added to the list of successful anastomoses.

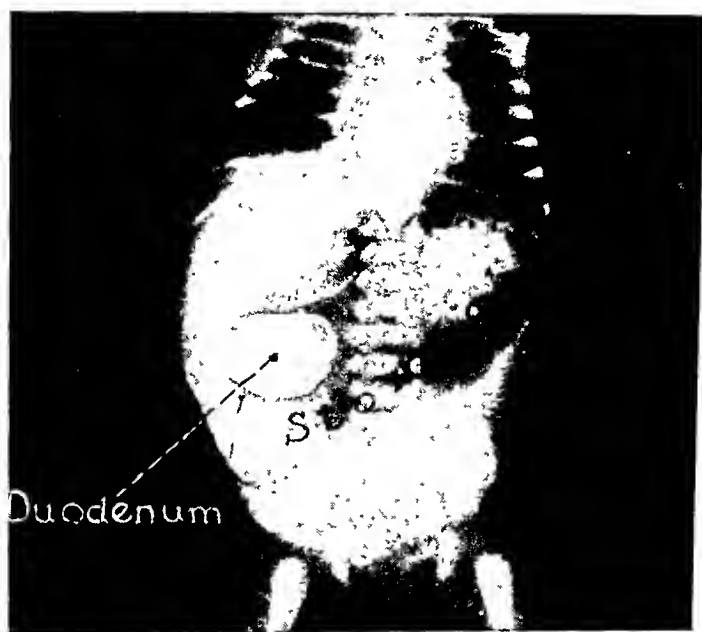


FIG. 1.—Barium study of stomach showing markedly dilated stomach and duodenum.

Case Report.—The patient was a 3.08-kilogram newborn female who, upon examination at birth, revealed no abnormalities. Breast feedings and dextrose water by mouth were begun six hours after birth. Meconium was normal in appearance. When 36 hours old the patient began to vomit dark brown viscid material, and upper abdominal distension, without visible peristalsis, appeared. Her appetite continued unimpaired. A plain film of the abdomen revealed a greatly dilated stomach but no gas in the small intestine. Barium administered by mouth was found to fill the stomach and proximal duodenum, but none passed beyond the obstructed point (Fig. 1). A barium enema showed the position of the colon to be normal. *Clinical Diagnosis:* Congenital obstruction of the duodenum. To combat the dehydration, a constant intravenous drip of dextrose and plasma was begun immediately. The contents of the stomach were aspirated through a small rubber catheter.

ATRESIA OF DUODENUM

Operation.—At the age of five days, under drop-ether anesthesia, the abdomen was entered through a right rectus, muscle-splitting incision. The stomach and proximal duodenum were markedly dilated. There was a complete atresia in the second portion of the duodenum with the duodenum represented by a fibrous cord for a distance of two centimeters (Fig. 2a). The impression was that the atresia was distal to the papilla of Vater. Because of the size of the structure, the common bile duct was not identified. The remaining intestine was collapsed and in normal position. No bile was seen when the distal intestine was opened. An anastomosis was performed between the end of the dilated second portion of the duodenum and the side of the third portion (Fig. 2b).

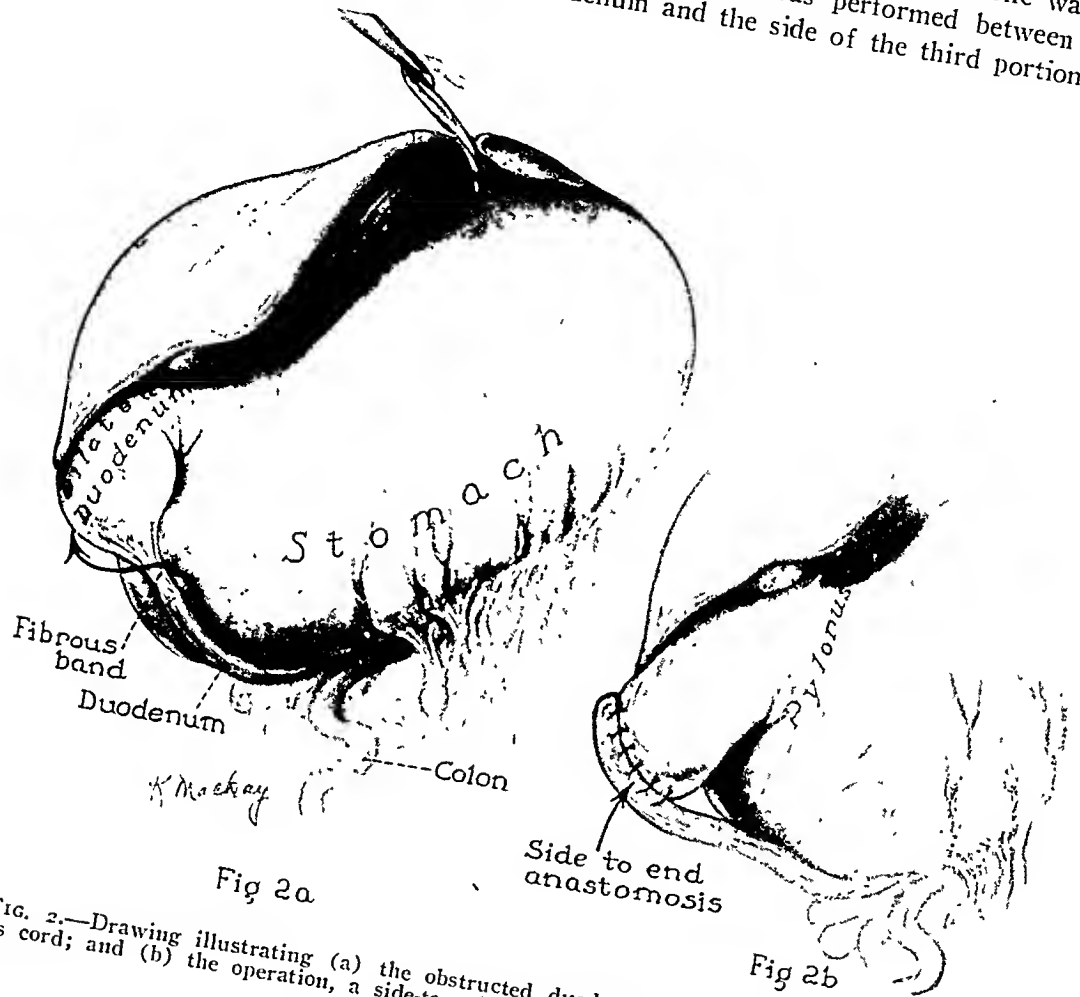


FIG. 2.—Drawing illustrating (a) the obstructed duodenum with the intestine represented by a fibrous cord; and (b) the operation, a side-to-end anastomosis, which was performed.

The anastomosis consisted of two layers of sutures: (1) An external layer of interrupted No. 1 silk serosal Lembert sutures; and (2) a continuous internal No. 00000 chromic catgut suture including all layers. The peritoneum was closed with a continuous No. 00 chromic catgut suture and the remainder of the wound closed in layers with interrupted black silk.

Postoperative Course.—Plasma and fluids were continued intravenously and the stomach was aspirated at frequent intervals. On the third postoperative day dextrose water was given by mouth and the following day a milk formula. There was occasional vomiting during the next four days. The plasma protein level was 4.3 Gm. per cent. After the administration of plasma the vomiting ceased. A barium study of the stomach demonstrated a functioning anastomosis (Fig. 3). The recovery thereafter was uneventful.

Follow-Up.—At the age of three months barium studies showed no duodenal obstruction nor delayed emptying of the stomach. Weight gain and development were normal.

DISCUSSION.—The fourteen successfully treated cases of proven complete obstruction of the duodenum are detailed in Table I, together with the site of obstruction and the type of operation performed. It is generally agreed that if the occlusion of the duodenum is above the papilla of Vater a gastro-enterostomy is the least formidable procedure. However, if the atresia is below the papilla of Vater, a duodeno-enterostomy should be performed, for it is readily apparent that here a gastro-enterostomy would necessitate a reflux of bile and pancreatic secretions back through the pylorus into the stomach. If the pylorus does not readily permit this reflux, gangrene and perforation of the blind pouch may occur. The entire small bowel should be inspected at the time of operation because of the frequency of multiple anomalies of the intestine.



FIG. 3 —Gastro intestinal series showing functioning anastomosis.

Probably in no branch of surgery is the pre- and post-operative management of the patient so important as in these cases. A recent article, by Maris, McGuinness, Lee, Rhoads, and Lee,¹⁴ advocates the use of a metal-tipped gastroduodenal tube in cases of duodenal obstruction. Its greatest usage should be at the time of exploration in eliminating the possibility of terminating an operation before the lumen is patent. Frequently the distal bowel does not distend following the release of an obstruction enough to eliminate the possibility of a second obstructing point. If the metal-tipped tube is passed into the first portion of the jejunum at the time of operation, considerable postoperative difficulty may be avoided. The degree

of the patient's hydration should be carefully watched, and free use of plasma and blood should be made as indicated by the plasma protein and hematocrit determinations.

The diagnosis should be established as early as possible and operative intervention for the reestablishment of the continuity of the bowel delayed only for purposes of obtaining a better operative risk through hydration and transfusion of the patient.

Frequent aspiration of the contents of the stomach during the immediate

ATRESIA OF DUODENUM

postoperative period is a necessity because of the tendency of infants to swallow large quantities of air.
No report of a similar case in which a duodenoduodenostomy was successfully performed appears in the literature.

SYNOPSIS OF 15 SUCCESSFULLY TREATED CASES OF ATRESIA OF THE DUODENUM

Author	Age at Oper.	Sex	Site of Atresia	Operation Performed
1 Ernst, N. P. ¹ (1916)	11 days	M.	Below papilla of Vater	Duodenojejunosomy
2 Cutler, G. D. ² (1924)	4 days	Post.gastro-enterostomy
3 Richter, H. M. ³ (1924)	4 days	Post.gastro-enterostomy
4 Bolling, R. W. ⁴ (1926)	9 days	F.	Duodenojejunosomy, anterior to colon
5 Porter and Carter ⁵ (1927)	6 days	..	3rd portion duodenum	Not stated
6 Weeks, A. and Delprat, G. B. ⁶ (1927)	10 days	F.	3rd portion duodenum	Gastro-enterostomy
7 Sweet, G. B. and Robertson, C. ⁷ (1927)	9 days	..	At point where superior mesenteric crosses duodenum	Anterior gastro-enter- ostomy. Duodenoje- junostomy (21st day)
8 Donovan, E. J. ⁸ (1936)	4 days	..	3rd portion duodenum	Duodenojejunosomy, ant. to colon
9 Morton, J. J. and Jones, T. B. ⁹ (1936)	12 days	F.	2nd portion duodenum	Post. gastro-enter- ostomy
10 Morton, J. J. and Jones, T. B. ¹⁰ (1936)	8 days	..	At point crossed by superior mesenteric vessels	2mm.-thick diaphragm removed by cautery
11 Miller, E. M. ¹¹ (1939)	3 days	M.	Duodenojejunal junction	Duodenojejunosomy (transcolic)
12 Stetten, DeWitt ¹² (1940)	11 days	F.	2nd and 3rd portion of duodenum	Duodenojejunosomy
13 Fegetter, S. ¹³ (1940)	Post. gastro-enter- ostomy
14 Ladd, W. E. and Gross, E. G. ¹⁴ 9325	5 days	F.	2nd portion duodenum below papilla of Vater	Gastrojejunosomy
15 Present report				Duodenoduodenostomy

SUMMARY

A case of complete congenital atresia of the duodenum successfully treated by duodenoduodenostomy is presented.

REFERENCES

- ¹ Ernst, N. P.: A Case of Congenital Atresia of the Duodenum Treated by Operation. Brit. Med. Jour., 1, 644, 1916.
- ² Cutler, G. D.: Cited by Clara Loitman, Congenital Occlusion of the Intestine. Boston Med. and Surg. Jour., 197, 21, July, 1927.
- ³ Richter, H. M.: Abt's. Pediatrics, W. B. Saunders, Philadelphia, 3, 512, 1924.
- ⁴ Bolling, R. W.: Complete Congenital Obstruction of the Duodenum, Duodenojejunostomy at Nine Days. ANNALS OF SURGERY, 83, 543, 1926.
- ⁵ Porter and Carter: Cited by Clara Loitman, Congenital Occlusion of the Intestine. Boston Med. and Surg. Jour., 197, 21, July, 1927.

- ⁶ Weeks, A., and Delprat, C. B.: Congenital Intestinal Obstruction: Atresia of the Jejunum. *Surg. Clin. N. Amer.*, October, 1927.
- ⁷ Sweet, G. B., and Robertson, C.: A Case of Congenital Atresia of the Jejunum with Recovery. *Arch. Dis. Child. New Zealand*, 2, 186, 1927.
- ⁸ Donovan, E. J.: Congenital Atresia of the Duodenum in the Newborn. *ANNALS OF SURGERY*, 103, 455, 1936.
- ⁹ Morton, J. J., and Jones, T. B.: Obstruction About the Mesentery in Infants. *ANNALS OF SURGERY*, 104, 864, 1936.
- ¹⁰ Miller, E. M.: Bowel Obstruction in the Newborn. *ANNALS OF SURGERY*, 110, 587, 1939.
- ¹¹ Stetten, Dewitt: Duodenojejunostomy for Congenital, Intrinsic: Total Atresia at the Duodenojejunal Junction. *ANNALS OF SURGERY*, 111, 583-596, April, 1940.
- ¹² Fegetter, S.: Congenital Duodenal Atresia. *Lancet*, 2, 188-189, August 17, 1940.
- ¹³ Ladd, W. E., and Gross, E. G.: *Abdominal Surgery of Infancy and Childhood*. Philadelphia: W. B. Saunders Co., 1941.
- ¹⁴ Maris, E. P., McGuinness, A. C., Lee, H. F., Rhoads, J. E., and Lee, W. E.: The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn. *ANNALS OF SURGERY*, 117, 348-354, March, 1943.

CONGENITAL ATRESIA OF THE COMMON BILE DUCT

CASE REPORT

ABRAHAM STRAUSS, M.D., CAPT. JOSEPH GROSS, M.C., U.S.A.,
AND
LT. SEYMOUR KYMAN, M.C., U.S.A.
CLEVELAND, OHIO

CREDIT for the surgical treatment of congenital atresia and stenosis of the bile ducts is given by Ladd to John Thomson⁶ and J. B. Holmes.² "In 1927, the operation was first performed successfully (by Ladd³) for the relief of congenital atresia of the bile ducts." Ladd and Gross⁴ have covered the subject thoroughly in their book "Abdominal Surgery of Infancy and Childhood." They report on 45 cases proved at operation or autopsy. Because of the type of anomaly, Ladd was able to relieve only nine by operation. The two operable types are those that have a normal gallbladder, cystic and hepatic ducts but a common duct that ends blind. The case reported herewith belongs to the second group. Ladd reported six of this type with two deaths. The ages of his cases, when referred to the hospital, varied from one week to 11 months, with an average age of three months. Although Ladd noted an abnormal bleeding tendency as a symptom in this condition, he stated his cases were free from this. Smith and Ball⁵ reported a case that died following continuous hemorrhage from the umbilicus. This was a prominent complication in the case herewith reported.

Case Report.—S. G., white, female, was born October 22, 1941, one month prematurely. Birth was normal. Weight, 2600 Gm. Because the infant did not take her food properly from birth, she was given 60 cc. of Ringer's solution every other day by infusions. At the same time it was noted that the baby was becoming jaundiced, which became more marked at the end of one week. On October 29, the baby evacuated a very bloody green stool. One ampule of vitamin K was administered. The following day 30 cc. of blood was given intravenously and 20 cc. into the buttock, followed by an infusion of 110 cc. of Ringer's solution. Again, the baby passed considerable blood in the stool, and blood dripped almost constantly from the rectum. On October 31 her temperature rose to 102° F. Fifty cubic centimeters of blood was administered intravenously, and 120 cc. of Ringer's solution by infusion, in two doses. The stool was pale yellow. During this time she was given kapectate, one-half dram every three hours; and sulfathiazole, one-half grain every six hours. Infusions and transfusions were then administered as follows:

Date	Ringer's Sol.	Blood	Other Medication
Nov. 1.....	70 cc.	50 cc. I. V.	Sulfathiazole and
Nov. 2.....	80 cc.	55 cc. into bone marrow	kapectate.
Nov. 3.....	25 cc.	25 cc. I. V.	Temp. 101.6° F.
Nov. 4.....	55 cc. into bone marrow	
Nov. 5.....	60 cc.	60 cc. into bone marrow	
Nov. 6.....	70 cc.	
Nov. 7.....	50 cc. into bone marrow	
Nov. 24.....	40 cc.		

From November fifth on, jaundice increased and stools were acholic. Weight remained 2500–2600 Gm. Bilton was started on November 6, 1941. Operative intervention was urged, hoping that the anomaly of the bile ducts could be remedied. The baby continued to have acholic stools, but did not bleed.

Operation.—November 26, 1941: Choledochoduodenostomy. Under open ether anesthesia, the abdomen was opened through an upper right rectus incision, splitting the rectus muscle. The liver itself was found to be considerably enlarged, extending approximately two fingers' breadth below the costal margin. The gallbladder appeared normal and tense. The common and cystic ducts were dilated. The common duct ended in a blind



FIG 1—Roentgenogram showing catheter in common duct and duodenum

point as it passed behind the duodenum. The condition representing a congenital atresia of the bile duct at its entrance to the duodenum. It was decided to perform a choledochoduodenostomy. A series of Deknatel "D" sutures were placed from the duodenum to a point in the common duct just above its tapering point, where a transverse incision was made in the common duct. This exposed its lumen. A No. 10 F. catheter, about two centimeters long, was then inserted into the common duct. Bile flowed from the open end of the tube. The sutures placed posteriorly were tied. A corresponding incision

CONGENITAL ATRESIA OF COMMON DUCT

was then made into the duodenum, and the free end of the catheter was inserted into the intestine (Fig. 1). Sutures were then placed in the anterior wall of the common duct and into the duodenum below the incision, and tied. This brought the duodenum and common duct together over the tube. This row of sutures was reinforced at each angle, and anteriorly, with similar interrupted Deknatel "D" sutures, thus completing a simple anastomosis between the common duct and duodenum. The abdominal wound was closed in layers with chromic No. 0, after first placing a series of through-and-through Deknatel No. 2 sutures.

On December 3, one week post-operative, the catheter that had been fitted into the common duct and duodenum was passed in the stool, which was still acholic. On December 6 the stool was light brown, but did not show positive test for hydrobilirubin until December 13. The jaundice of the skin and scleras was becoming paler. Convalescence was definitely handicapped by a severe bronchopneumonia and coryza that started on December 6. The infant was in a heated crib at all times. Oxygen and sulfathiozole were given until December 14.

The wound healed with only slight amount of serum and some separation of the skin edges, so that it finally healed superficially by granulation. The patient was discharged on December 21, on the 25th post-operative day, with very little jaundice and normal stools. At the end of one year she weighed 23 pounds.

Regarding the differential diagnosis and operability: Congenital atresia of the bile ducts must be differentiated from five other conditions presenting jaundice in the newborn:

1. In icterus neonatorum the jaundice usually disappears by the end of the second week. The liver is not enlarged and the stools contain bile pigment.
2. Erythroblastosis foetalis is usually fatal in the first few days or weeks of life. It is marked by jaundice, a large liver, and large spleen, and increased erythroblasts. It may be suspected from the golden-colored vernix caseosa and hypertrophied placenta.
3. Jaundice of hemolytic sepsis is differentiated by fever, leukocytosis, progressive anemia, toxicity, and no acholic stools.
4. Congenital syphilis may be identified by blood test and the roentgenologic appearance of the bones.

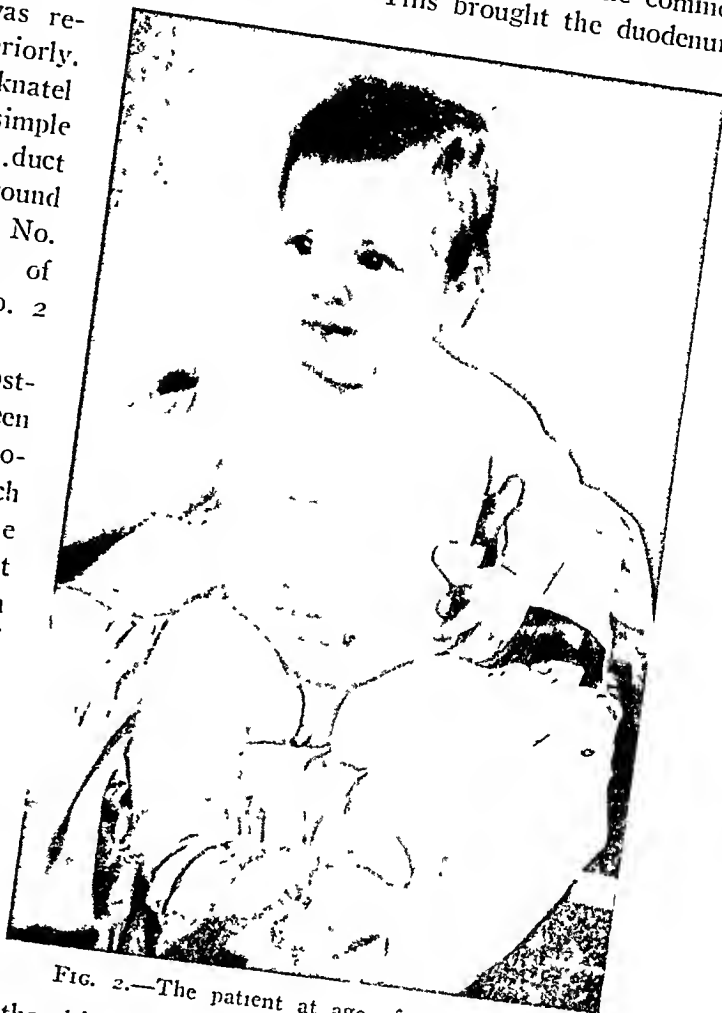


FIG. 2.—The patient at age of 10 months

CLINICAL LABORATORY REPORTS

	11/8	11/11	11/25	12/2	12/8	12/10
W.B.C.....	22,400	20,560	16,000	16,200	13,100	9500
R.B.C.	5 25	5 5	4 92	4 33		
Hb... ..	103%	107%	97 4%	80%	84.4%	78%

SPECIAL LABORATORY REPORTS

Specimen	Date	Report
Stool . . .	10/30	Occult blood—positive
Blood . . .	10/30	Hb—97.4% R.B.C.—5.18 W.B.C.—9850
Stool-culture	11/1	Culture-abundant growth <i>B coli</i>
Urine. . .	11/5	Bile—positive. Alb.—heavy tr. Sugar—neg. Reaction—neutral Microscopic—large no. bacteria, few pus and epith. cells, mod. amt. amorphous urates. Occult blood—neg.
Stool	11/5	Clay-colored, soft, unformed. Occult blood—very slightly positive. Hydrobilirubin—neg
Blood .. .	11/25	Bleeding time—1½ min. Clotting time 4 min. Hb—97.4%. R.B.C.—4.88 W.B.C.—10,900 Polys—28%. Lymphs—48%. Mons—6%. Eosin—18%; R.B.C. show slight variation in size. Platelets appear normal.
Stool . . .	12/1	Occult Blood—positive.
Stool.. . .	12/2	Bilirubin—neg.
Stool . . .	12/2	Light colored, yellowish, soft, unformed. Presence of bile—negative.
Stool . . .	12/1	Light colored, yellowish, soft, formed. Bilirubin, negative.
Stool . . .	12/2	Hydrobilirubin, negative. Occult blood, pos.
Stool . . .	12/3	Hydrobilirubin, negative.
Blood . . .	12/11	Polys—31%, lymphs—64%, mono—3%, eosin—2%. Nucleated red cells—1 R.B.C. show variation in shape. Few R.B.C. show basophilic stippling. Lymphs appear atypical. Platelets appear normal.
Stool . . .	12/9	Yellow, soft, formed, unaltered bilirubin.
Stool . . .	12/10	Yellow, soft, unformed, unaltered bilirubin.
Stool .. .	12/12	Yellow, soft, formed. Very slightly positive for unaltered bilirubin (bil-verdin).

5. Obstructive jaundice from inspissated bile or mucus may give a picture indistinguishable from atresia, and may require surgery for relief. There may or may not be normal stools in the beginning as this depends on when the duct becomes occluded.

Even in cases of atresia, jaundice may not be evident until a few weeks after birth, as is reported in a case by Feldman and Lawson.⁸ This infant died, age 12 weeks, weighing eight pounds. Jaundice was first noticed three weeks after birth. Postmortem examination revealed no gallbladder or cystic duct. The two small, thick hepatic ducts were present but no connection was found with the duodenum.

Watkins and Wright,⁷ in reporting their binovular twin that developed jaundice six or seven days after birth, with normal stools the first few days, later becoming pale; stated: "The absence of jaundice at birth and the presence of normal meconium during the first few days have been regarded as implying that the biliary tract in such cases is at least partially patent at birth. It should be pointed out, however, that bile pigment is not present in the biliary secretions until the fifth or sixth month of fetal life (Ylppo), and from then until birth only in small amounts. After birth, bile is produced in larger quantity, but should its flow be obstructed by impervious ducts, jaundice gradually develops. In other words, the delayed onset of the jaundice coincides with the much augmented production of bile in the first few days

CONGENITAL ATRESIA OF COMMON DUCT

after birth and does not necessarily imply there is a postnatal closure of the main biliary duct tract.”

One must not be misled by the color of the stools at birth. Although they may be yellow and appear normal, they will have no bile in them. Proved cases have shown that they may not become clay-colored until three to 14 days after birth.

We wish to emphasize these points because the physician may feel loathe to urge operation on certain cases of atresia that may be operable if he believes that jaundice from birth is a *sine qua non* of atresia. Thus, infants have been allowed to die, only to find postmortem that they had an operable condition. Ladd writes that, as a rule, if one delays in making the diagnosis of atresia for four to six weeks the chance of error is not great. Further delay serves no good purpose but does lower the resistance of the child so that operation may then be fatal.

Operation should be urged in atresia in spite of the fact that only 17 to 20 per cent will be operable. Ladd reported nine operable cases out of 45, with three operative deaths, and one who died four months later. Donovan had one recovery.

The case reported herewith is the seventh recorded successful operation for atresia of the bile ducts.

REFERENCES

- ¹ Donovan, E. J.: Congenital Atresia of the Bile Ducts. *ANNALS OF SURGERY*, 106, 737, 1937.
- ² Holmes, J. B.: Congenital Atresia of the Bile Ducts. *Am. Jour. Dis. Child.*, 11, 405, 1916.
- ³ Ladd, W. E.: Congenital Atresia of the Bile Duct and Stenosis of the Bile Ducts. *J. A. M. A.*, 91, 1082; 1928; *idem*: Congenital Obstruction of the Bile Ducts. *ANNALS OF SURGERY*, 102, 742, 1935.
- ⁴ Ladd and Gross: *Abdominal Surgery of Infancy and Childhood*. W. B. Saunders Co., Philadelphia, 1941.
- ⁵ Smith, T. Cook, and Ball, Robert T.: Congenital Obliteration of the Gallbladder with Atresia of the Extrahepatic Bile Ducts and Ampulla of Vater. *Kentucky Med. Jour.*, 27, 252, 1929.
- ⁶ Thompson, John: On Congenital Obliteration of the Bile Ducts. *Edinburg Med. Jour.*, 37, 523, 1892.
- ⁷ Watkins, A. G., and Wright, G. Payling: Congenital Atresia of the Bile Ducts. *Lancet*, 224, 1066, 1933.
- ⁸ Feldman, W. M., and Lawson, Miriam A.: A Case of “Congenital” Occlusion of the Common Hepatic Duct. *The Lancet*, 207, 113, July 19, 1924.

CYST OF THE AMPULLA OF VATER

CASE REPORT

BARNEY BROOKS, M.D., AND ALBERT WEINSTEIN, M.D.

NASHVILLE, TENN.

FROM THE DEPARTMENTS OF SURGERY AND MEDICINE, VANDERBILT UNIVERSITY, NASHVILLE, TENN.

Case Report.—Vanderbilt University Hospital No. 119392: A white male, age 30, was admitted to the hospital, February 2, 1942, because of repeated attacks of abdominal pain accompanied by nausea, vomiting and possibly jaundice. Although the patient emphasized the symptoms which had been present for the past year, he was able to give a detailed account of an illness occurring at the age of 15, characterized by severe epigastric pain and tenderness, nausea and vomiting, of a sufficient intensity to lead a physician to make a diagnosis of acute cholecystitis, perform of celiotomy and place a drainage tube in the gallbladder. Following the removal of this tube, the patient made an uninterrupted recovery and considered himself well until he was 26 years old, at which time he began to suffer from hemorrhoids, for which an operation was performed in February, 1941.

Approximately one month after this operation the patient had an attack of pain, deeply boring in character and entirely confined to the epigastrium. The pain reached its climax in four or five hours and was accompanied by nausea and vomiting. The symptoms persisted for about 24 hours, after which he considered himself well for a period of one month, when he experienced a similar episode.

These attacks have subsequently occurred approximately once each month. Neither the patient nor his family have noticed any discoloration of the skin or sclera, but the patient believes that his urine became dark in color after at least some of his attacks.

Ten months before admission the patient saw a physician, who made a diagnosis of peptic ulcer. On January 1, 1942, the patient began the use of the Muelengracht diet, to which regimen he has carefully adhered, without obtaining relief. His weight decreased from 190 to 150 pounds. The patient experienced his last attack approximately one week before being admitted to the Vanderbilt University Hospital.

On admission to the hospital the patient appeared as a fairly well nourished, intelligent, cooperative individual. Examination of the abdomen was particularly satisfactory because of the unusual relaxation of the abdominal wall, and no abnormalities of the abdomen were detected. The usual microscopic and chemical examination of the blood and urine showed no abnormality except for the elevation of the icteric index to 12 units, following one episode of pain. Repeated examination of the stools always disclosed the presence of occult blood. Cholecystographic examination showed a definite but faint shadow of the gallbladder.

Roentgenologic examination of the gastro-intestinal tract by means of the barium meal was of particular interest because of our failure to observe in the roentgenograms definite evidence of the unusual lesion subsequently disclosed at operation. The dilatation of the duodenum and proximal portion of the jejunum was quite obvious, but the curious filling defect in the duodenum, as shown by Figures 1 and 2, was not seen until after operation.

Operation.—February 12, 1942: The abdomen was opened to the right of the midline above the level of the umbilicus. It was noted that the gallbladder was completely obscured by adhesions, and the operator turned his attention first to an examination of the jejunum. Approximately the first two feet of the jejunum showed marked hypertrophy and dilatation. The walls of the intestine were thick and

CYST OF AMPULLA OF VATER

leathery and the hypertrophy of the longitudinal muscle coat of the intestine was such as to produce gross striation. The hypertrophy and dilatation terminated almost abruptly into normal small bowel, without any evidence of obstruction at the point of termination. Examination of the stomach and first portion of the duodenum showed nothing abnormal except for small stellate scarring of the anterior wall of the duodenum just distal to the pylorus. There was, however, in the scar no induration or other evidence of duodenal ulcer. About one inch from the pylorus the duodenum became



FIG. 1—Roentgenogram after ingestion of barium meal showing dilated duodenum with large filling defect. (See Figure 2.)

greatly enlarged. The enlargement was such that the diameter of the duodenum was approximately the same as that of the stomach. On palpation, the duodenum was tense and fluctuant. When pressure was first exerted upon the tense duodenum, it could not be made to collapse, but subsequently, while handling the duodenum, the operator was aware of an abrupt partial emptying of the distended duodenum in the direction of the jejunum, which immediately became distended with fluid. Further attempts to empty the duodenum were unsuccessful. An incision was then made in the posterior peritoneum along the lateral wall of the duodenum, which, thus mobilized, was delivered into the operative wound. A longitudinal incision approximately ten centimeters in length, was then made through the anterior duodenal wall. The duodenum was found to contain a large polypoid mass which, when delivered through the incision in the duodenum, was found to be attached to the posterior wall of the descending portion

of the duodenum. The polypoid mass was estimated as measuring 8 cm. in diameter and 12 to 15 cm. in length—(note the mass was considerably reduced previous to the opening of the duodenum). The operator observed that if the tumor was stretched towards the left, it was sufficiently long to reach for some distance beyond Treitz' ligament. The entire polypoid mass was covered with what appeared to be normal duodenal mucosa. At the apex of the tumor there was a slit-like opening which, after

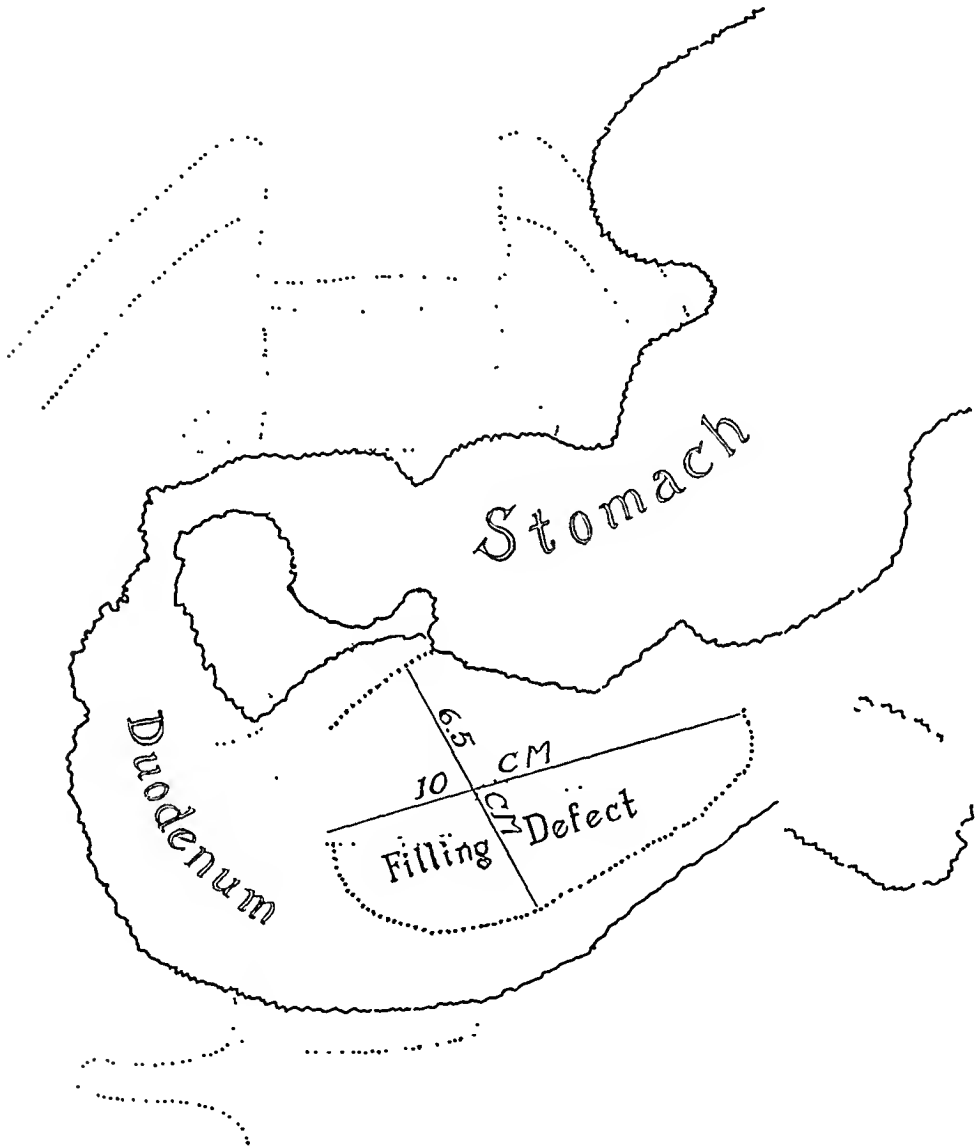


FIG. 2.—Tracing of roentgenogram shown in Figure 1.

its edges were separated, permitted the discharge of a large amount of golden-yellow bile. If the edges of the slit were not held apart, a considerable amount of pressure could be exerted upon the tumor without causing the discharge of bile (Fig. 3).

An incision was made through the anterior aspect of the tumor and it was found that the central portion of the tumor was occupied by a cavity lined with mucosa, which had the same appearance as the mucosa of the duodenum. On careful examination it was noted that there were two small openings into the central cavity. These openings were approximately two millimeters apart, one being slightly larger than the other. A probe passed into the larger opening followed the pedicle of the tumor

CYST OF AMPULLA OF VATER

into what appeared to be quite normal common bile duct. A probe passed into the other opening apparently followed the direction of the duct of Wirsung. The cavity within the polyp communicated with the lumen of the duodenum by means of a slit-like opening at the tip of the tumor (Fig. 4).

A circular incision was made about the apertures of the common bile duct and pancreatic duct (Fig. 4), and all of the mucosa lining the central cavity except that contained within the circular incision was removed. The greater portion of the mucosa covering the polypoid mass was then removed. This resulted in what appeared to be

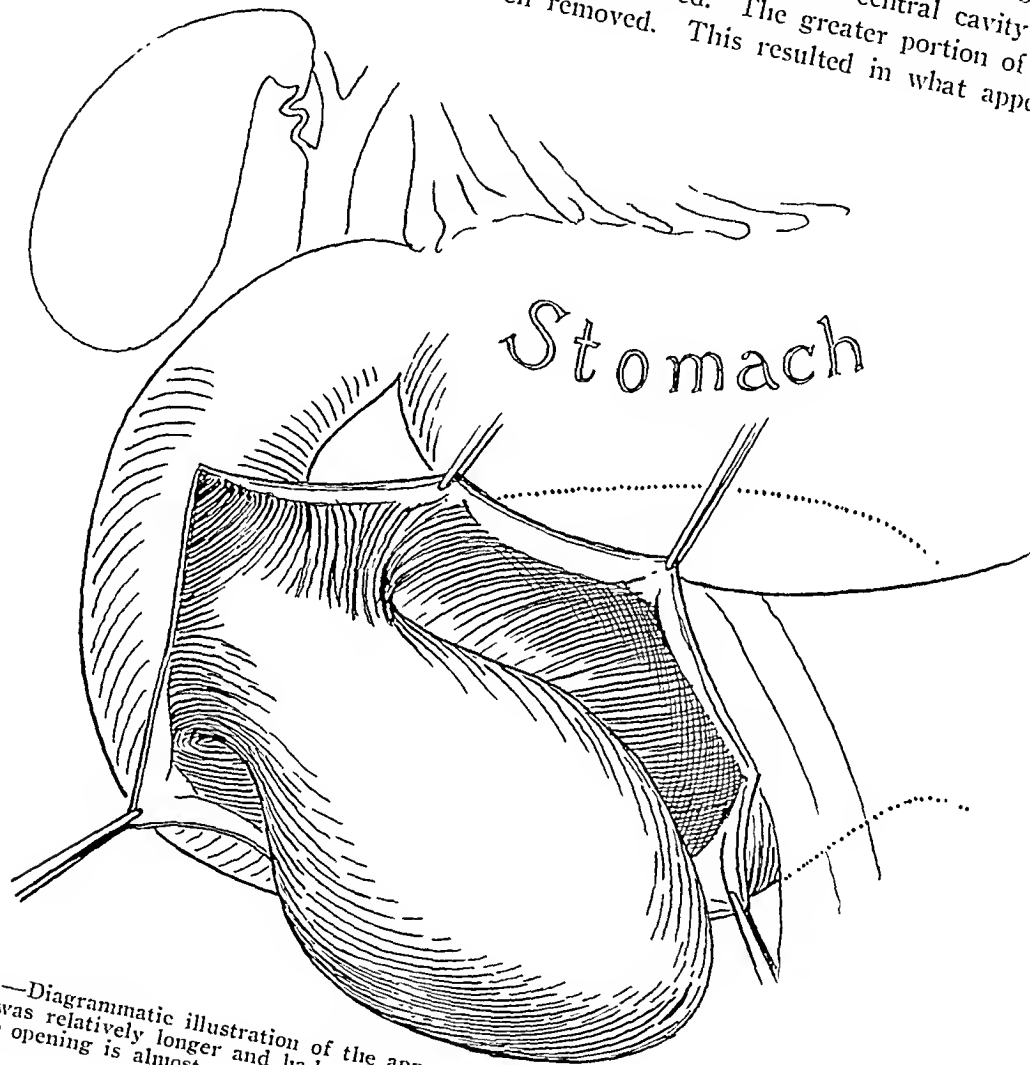


FIG. 3.—Diagrammatic illustration of the appearance of the duodenum after it was opened. The polyp was relatively longer and had a more bulbous tip than is shown in this illustration. The slit-like opening is almost as obscure in the illustration as it was in reality.

a linear incision of the mucosa of the posterior wall of the duodenum, within which there was a separate island of mucosa derived from the mucosal lining of the central cyst. The mucosa of the posterior wall of the duodenum was then closed, incorporating the island of mucosa surrounding the openings of the bile and pancreatic ducts (Fig. 5). The incision in the anterior wall of the duodenum was then closed by a double row of inverting sutures.

The gallbladder was then exposed by separation of the surrounding adhesions, and, on palpation, was found to contain a few small stones. An incision was made at the tip of the gallbladder and the stones removed. The operator hesitated to remove the gallbladder for fear that a subsequent constriction would form at the opening of the common bile duct into the duodenum. A small tube was, therefore, placed in the fundus of the gallbladder and brought out through a stab wound at the right costal margin. The abdominal incision was closed in layers.

The patient's postoperative course was uneventful. He was discharged from the hospital on the 12th postoperative day. During the year following operation the patient has enjoyed excellent health, and has gained 40 pounds. When reexamined a year after operation he appeared to be in perfect physical condition. At this time roentgenologic examination of the gastro-intestinal tract revealed slight dilatation only of the upper portion of the jejunum, with no evidence of obstruction.

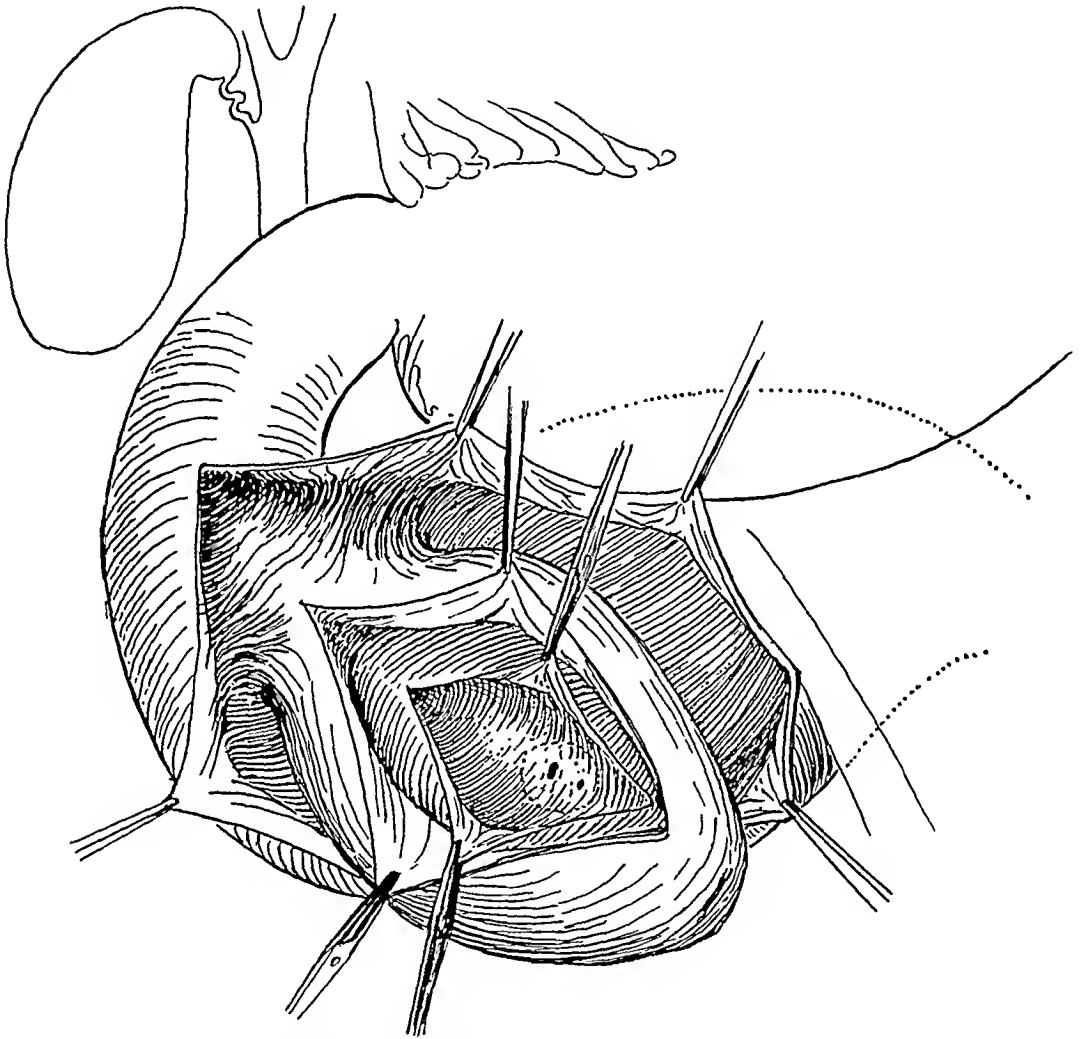


FIG. 4.—Diagrammatic illustration of the appearance of the polypoid tumor after an incision was made into the central cyst. The dotted line around the apertures of the bile and pancreatic ducts marks the site of the incision made for preserving this area of mucosa for subsequent transplantation into the posterior duodenal wall.

DISCUSSION

The term, cyst of the ampulla of Vater, is used in the title of this paper because it seemed best suited for making this report available in the current medical indices to those subsequently interested in this subject, but in reality the conditions present were not as simple as this term implies.

Whatever the cause of the initial anomaly at the normal site of the ampulla of Vater was, it seems quite certain that the outstanding anatomic characteristics of the tumor, the duodenum and proximal jejunum, as well as the

CYST OF AMPULLA OF VATER

major symptoms present, were because of the intussusception of the cyst. In fact, it is difficult to understand how so large a mass could exist in the duodenum without more discomfort than the patient appeared to have. The hypertrophy of the jejunum for a distance greater than the length of the tumor is easily accounted for by the bulbous end of the tumor, which if once engaged in peristaltic waves would result in the jejunum being drawn on to the intussuscepted mass after its further progress were impossible because of the attachment of its pedicle.

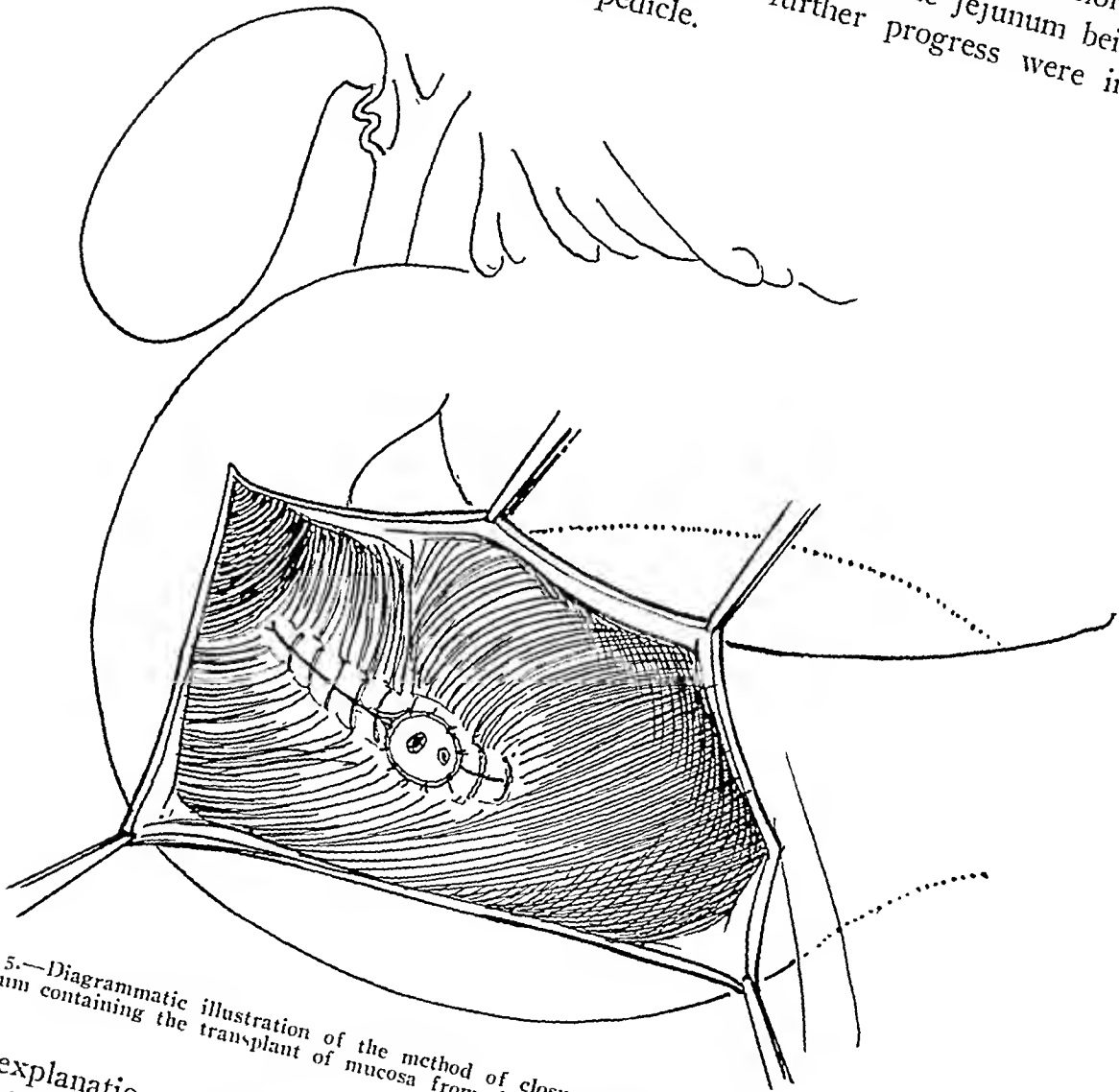


FIG. 5.—Diagrammatic illustration of the method of closure of the wound in the posterior wall of duodenum containing the transplant of mucosa from the central cyst.

The explanation of the initial anomaly is by no means as simple as the title of this report implies. Although the slit-like opening in the distal end of the polypoid tumor seemed quite analogous to the aperture of the normal ampulla of Vater, and the common bile duct and the duct of Wirsung opened into the cyst, it appeared impossible to consider the cyst as having been acquired from a dilatation of the canal within the ampulla, because the slit-like opening of the cyst into the duodenum was really larger than the aperture of the normal ampulla, and because the cyst was lined with a mucosa which, on both gross and microscopic examination, was identical with the

normal mucosa of the duodenum. Also, the openings of the bile and pancreatic ducts were at the distal aspect of the cyst.

It appears, therefore, as if the abnormality described herewith was a congenital anomaly of the duodenal wall and not an acquired dilatation of the ampulla of Vater. The authors were unable to find a record of a similar condition having been observed except perhaps the "anomalous pouch" of the duodenum reported by J. C. Boileau Grant.¹

The nature of the symptoms experienced by the patient at the age of 15, is strongly presumptive evidence of the existence of the polypoid tumor at that time. In this connection, it is interesting to note the remarkable change in the patient's definition of being "well" before and after operation. Before operation the patient believed himself "well" between "attacks of severe pain, nausea and vomiting" only occurring during the year previous to operation. One year after operation he stated that he had, since the operation, enjoyed a feeling of comfort and well-being previously unknown to him.

REFERENCE

- ¹ Grant, J. C. Boileau: Anomalous Duodenal Pouch. *Brit. Jour. Surg.*, 23, 233, July, 1935.

HYPERESTHESIA OF THE POSTERIOR PERITONEUM (Objective Pain) IN APPENDICITIS AND OTHER VISCERAL LESIONS

RAFAEL CAPURRO, M.D.

MONTEVIDEO, URUGUAY

FROM THE SURGICAL SERVICES OF THE MILITARY HOSPITAL, THE SOCIEDAD ESPANOLA, AND THE SANATORIO OBRERAS Y EMPLEADAS, MONTEVIDEO, URUGUAY.

IN A SERIES of cases of appendicitis, we have been brought to consider that there exists a zone of objective pain in the region of the iliacus muscle (Plate I, Fig. 3). These cases included chronic and acute appendicitis, with little or no spasticity of the abdominal wall (such as catarrhal or diffuse appendicitis, with a weak peritoneal reaction). That is to say, that the deep palpation of this area just internal *to* and *above*, the crest of the anterior iliac spine provokes a pain that is quite localized (Fig. 1). This painful reaction is completely independent of the position of the appendix. It facilitates the diagnosis and in certain cases determines it.

In October, 1941, we had the opportunity to utilize the advantages of local anesthesia in performing direct palpation of the iliacus muscle with the finger tip (Plate I, Fig. 1). In a case of catarrhal appendicitis a reaction was elicited by touching the external interior portion of iliacus muscle in the same manner as clinical palpation and elicited an earlier painful response. A logical deduction was that if there was a zone of objective sensitivity determined by the lesion in the appendix; the anesthesia of the meso-appendix with novocain should eliminate this hyperesthesia by blocking the sympathetic pathway (Plate I, Fig. 2).

On the same day we operated upon two cases of appendicitis. One, a diffuse, acute appendicitis, with a weak peritoneal reaction; the other, an appendicitis of long standing, with recurring attacks. In both cases there was an objective painful response on palpation of the iliacus muscle region which disappeared in each of the two cases after injection of one per cent novocain into the meso-appendix.

These observations were continued until 53 cases had been checked by our own and other surgeons' observations. In all but one of these the results were positive. The exception gave evidence of objective pain on external palpation but upon operating we were unable to elicit the painful response area by direct digital palpation. It is possible that the diffuse anesthesia of the abdominal wall in this case may explain this aberrant result.

At this stage of our investigation we considered the probability that if lesions of the appendix provoked hyperesthesia in the posterior abdominal wall, then it was possible that lesions of other organs might induce hyperesthesia in other regions of the posterior abdominal wall. This line of reasoning was subsequently investigated as follows:

In salpingo-oophoritis we found the zone of hyperesthesia to be on the body of the first sacral vertebra near the sacral wing. Right or left according to the site of location of the lesion. It would be difficult with local anesthesia to operate upon a case of salpingo-oophoritis and to palpate the region directly, and thus cause the disappearance of pain by novocain injection of the mesosalpinx and mesovarium. However, in lesions of the external genitalia of the male (epididymitis) the same area of hyperesthesia was found as

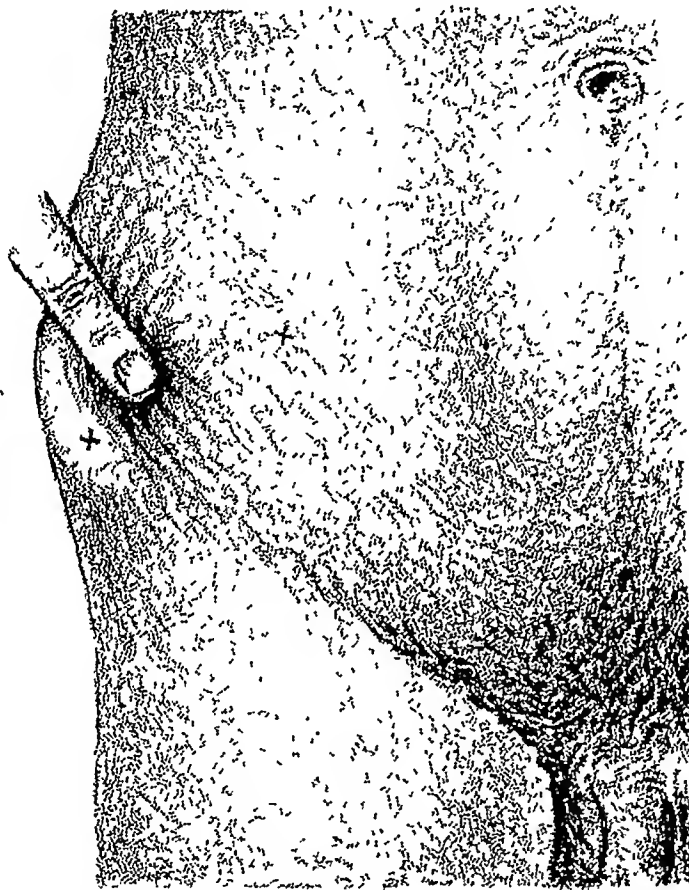


FIG. 1.—Deep palpation of the abdomen about 2 cm medial and 2 cm superior to the anterior iliac spine. Objective pain is diagnostic of a lesion of the appendix. x marks McBurney's point.

for salpingo-oophoritis. This reflex pain disappeared after novocain infiltration of the scrotal cord.

In looking for the areas of hyperesthesia in lesions of the stomach, duodenum, and gallbladder; they appear, from our few observations, to be on the bodies of the lumbar vertebrae at the level of the umbilicus. In kidney lesions the zone appears to be on the iliac crest at the anterior axillary line, and is lateral to the ureter.*

Returning to the study of appendicitis, we were faced with the question of the location of the seat of pain. Is it in the iliacus muscle or in the peri-

* This much of our work was presented before the "Surgical Society of 'Montevideo'" in April, 1942.

HYPERESTHESIA IN APPENDICITIS

toneum which covers it, or possibly the femoral cutaneous nerve? The extent of the pain area eliminates the possibility of direct compression of the nerve as being responsible. McKenzie has described a reaction of sensitivity in the iliopsoas muscle in lesions of viscera whose innervation corresponds to the metameric 11th or 12th thoracic segments. He did not mention special localization in specific zones for specific organs.

We had the opportunity of performing three experiments that suggested that the pain area appeared to be in the peritoneum and not in the muscle: In these three cases of appendicitis, operated upon under local anesthesia, we carefully freed the peritoneum from the surface of the iliacus muscle (Plate I, Fig. 4). Digital pressure on the muscle induced no painful response, whereas compression of the peritoneum between two fingers one extra- and the other intraperitoneal, provoked the painful reaction which, in turn, was eliminated by novocain infiltration of the meso-appendix.

PHYSIOPATHOLOGY

The results we have described follow the accepted explanation of objective painful reflex responses. One must remember that the visceral peritoneum receives its innervation from the thoracolumbar sympathetic and from the craniosacral parasympathetic systems. On the other hand, the parietal peritoneum is innervated by the spinal nerves. In the case of a lesion of the appendix, the visceral afferent nerves convey impulses to the spinal cord, and connections are made with efferents of the 11th and 12th thoracic segments, which are those involved in the innervation of the parietal peritoneum covering the iliacus muscle. Injection of novocain into the meso-appendix eliminates the reflex at its source.

Clinical application of this test has been made by myself and other surgeons in 200 cases. The physical examination of patients with appendicitis, with little or no abdominal spasticity, have been made as follows:

CLINICAL APPLICATION

- (1) Palpation of the anterior wall of the iliac fossa (McBurney).
 - (2) Visceral palpation to make direct contact with the cecum and appendix in order to determine the presence or absence of pain in this organ. Distinction is made between visceral and anterior abdominal wall pain by the well known procedure of an attempt by the patient to raise himself.
 - (3) Deep palpation of the iliac fossa, as described previously: It is necessary to use all four fingers at first. When the zone of hyperesthesia has been found, an index finger is sufficient for the subsequent palpation. Frequently the cecum can be displaced and, also, the edge of the psoas can be felt, and the area more sharply defined.
- The facts obtained by these observations can be schematically applied:
- (1) Acute catarrhal appendix, or diffuse type, with little peritoneal reaction:

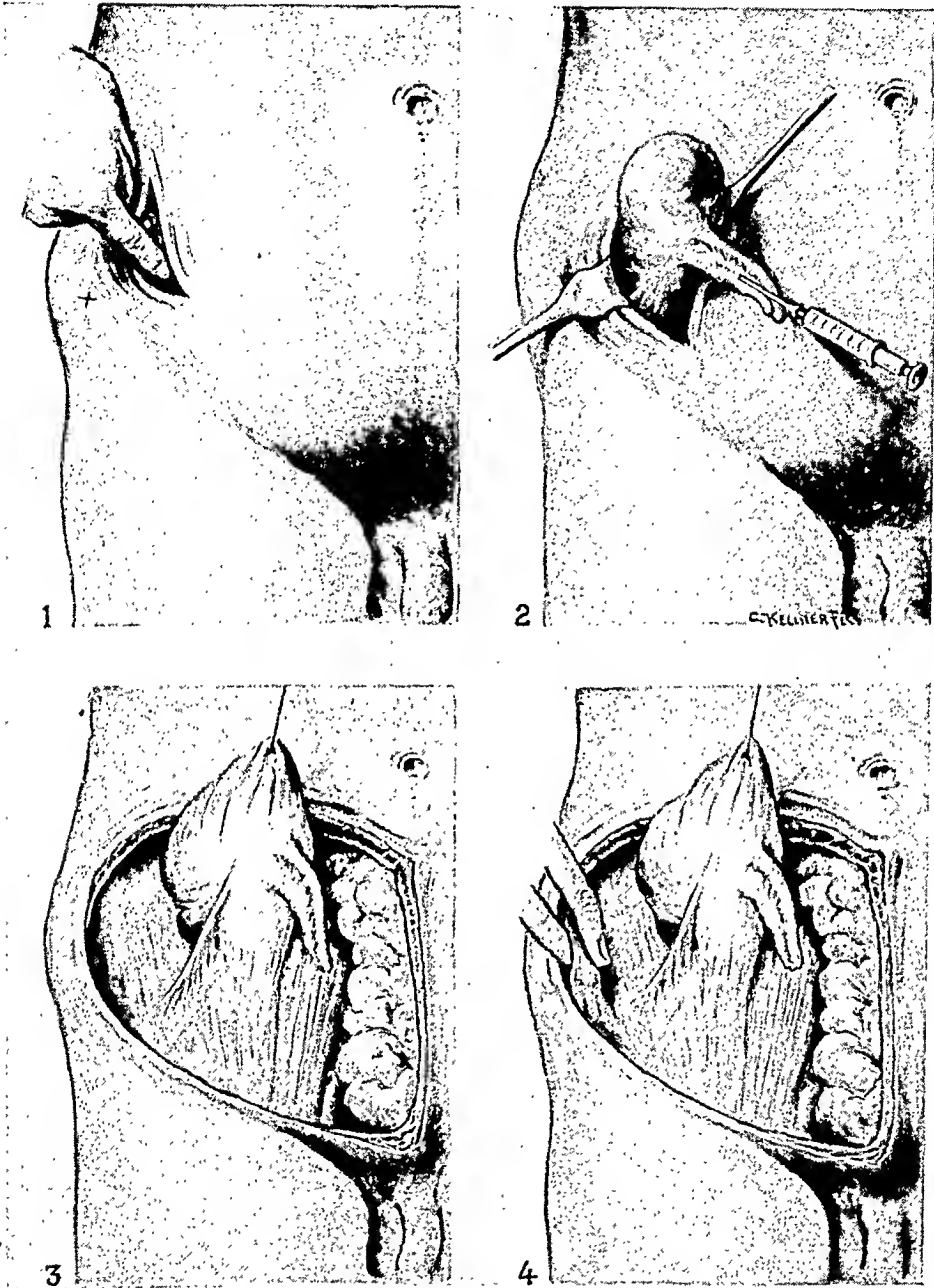


PLATE I, FIG. 1.—Direct pressure on the posterior parietal peritoneum covering the iliac fossa: If objective pain is elicited, it can be blocked by infiltration of the meso-appendix with novocain as indicated in Figure 2.

FIG. 2.—The cecum and appendix are brought out of the incision and about 3 cc. of 2% novocain is injected into the meso-appendix.

FIG. 3.—Anatomic exposure of the iliac fossa showing the area of hyperesthesia.

FIG. 4.—During operation the posterior, parietal, and abdominal peritoneum can be freed, so that pressure can be applied to the muscle directly, or to the peritoneum, between two fingers, as shown. The same pressure after novocain has been injected into the meso-appendix elicits no objective pain.

(a) Appendix in normal situation or position. McBurney point apparent; a painful appendix, and an hyperesthesia of the posterior parietal peritoneum. In these cases the test confirms the diagnosis. When McBurney's point tenderness is little apparent, the test has greater diagnostic aid.

HYPERESTHESIA IN APPENDICITIS

(b) Abnormal position of the appendix, retrocolic with high cecum: Pain in the flank near the right lumbar region or in the right hypochondrium, with weak McBurney reaction, but with a clear reaction on the posterior peritoneum. In these cases the value of the test is in the differential diagnosis from renal and gallbladder lesions. A similar value appears in the case of the pelvic appendices in order to distinguish them from genital lesions.

(2) In recurring or chronic appendicitis our test should be *more* important. We have observed cases in which appendices without pain were examined radiologically. The existence of our positive test permitted the diagnosis of appendicitis, which was subsequently confirmed by operation. One must realize that in obese and neurotic patients, and in those with hypersensitivity of the sympathetics, the deep palpation test is not possible.

Our impression is that the hyperesthesia of the posterior parietal peritoneum is more persistent than that of the anterior wall, and is, therefore, maintained in lesions of long standing. The negative result with external palpation, found only in one case out of our 200 cases of true appendicitis, might be related to a retraction of the peritoneum toward the midline found upon operating. Dr. George Pitkin, of Teaneck, N. J., reported he had successfully employed this new diagnostic procedure in a case of acute appendicitis in which there appeared no painful reaction in the anterior wall (McBurney).

Of course, experience with the test is far from complete. We do not know, for instance, its results in general infections such as typhoid, influenza, purpura, rheumatism, *etc.* Nevertheless, it may enable one to increase the percentage of positive diagnoses, and, finally, we believe that the facts we have observed have a clinical and physiopathologic significance that merits further investigation.

The author wishes to thank coworkers Doctors P. A. Barcia, C. Menendez, R. Ardao, G. Herrera, and H. Scoseria, of Montevideo, Uruguay, and Dr. R. H. Zwemer of New York City, New York, for their assistance and cooperation in the preparation of this article.

METABOLIC STUDIES IN PATIENTS WITH CANCER OF THE GASTRO-INTESTINAL TRACT. XII—THE GLYCINE TOLERANCE TEST IN PATIENTS WITH GASTRIC CANCER*

IRVING ARIEL†, M.D., FLORENCE JONES, B.A., GEORGE T. PACK, M.D.,

AND

C. P. RHOADS, M.D.

NEW YORK, N. Y.

FROM THE MEMORIAL HOSPITAL, NEW YORK, N. Y.

AN EARLIER COMMUNICATION of this series¹ indicated that 59 per cent of patients with gastric cancer develop hypoproteinemia. This abnormality may be due to (a) the increased protein catabolism of these individuals; (b) their impaired ability to fabricate serum protein; or (c) simply an inadequate intake and absorption of dietary nitrogen constituents. Previous investigations² of nitrogen excretion as the cause of hypoproteinemia in patients bearing gastric cancer failed to demonstrate that their rate of tissue breakdown was increased. However, evidence was found which strongly suggested that these individuals no longer could synthesize serum albumin in normal amounts.¹

Since the presence of gastric cancer conceivably could influence the motility of the alimentary tract, it was possible that that abnormality impaired the absorption of nitrogenous foodstuffs and thus contributed to the development of the hypoproteinemia in these instances. The association of gastro-intestinal disorders with impaired absorption resulting in states of deficiency has been stressed by others.³ The present study was undertaken, therefore, to ascertain whether or not the usual end-products of protein digestion, *i.e.*, the amino-acids, were absorbed normally from the intestinal tract of patients with gastric cancer.

Methods.—Throughout the present investigation, the glycine tolerance test described by Erf and Rhoads⁴ was used. Samples of oxalated blood for the determination of plasma amino-acid nitrogen⁵ were obtained from the fasted patient at 0, 1, 2, 3, and 4 hours after his ingestion of 25 Gm. of glycine in 500 Ml. of water.

The urea content of the samples taken at 0, 2, and 4 hours after glycine feeding was measured by the technic of van Slyke.⁶

The urinary output of amino-acid nitrogen was measured for one day before, and for two days after, the administration of glycine. These determinations were made by the method of van Slyke, *et al.*⁵

Clinical Material.—The clinical material employed in this investigation were all adults and can be divided into four groups:

* The authors gratefully acknowledge the grant from the National Cancer Institute.

† Trainee in diagnosis and treatment, National Cancer Institute Fellow.

METABOLISM IN GASTRIC CANCER

- (A) Six patients who were used as controls. They all had neoplastic lesions of the extremities.
- (B) Six patients with gastro-intestinal cancer—five with adenocarcinoma of the stomach, and one with squamous cell cancer of the terminal esophagus. In all instances the diagnosis was proven by microscopic examination of biopsied material.
- (C) Three patients with non-neoplastic gastric lesions—one had multiple ulcers, the second had multiple polypi, and the third suffered from diffuse Boeck's sarcoid. The diagnosis was made in these individuals by celiotomy and microscopic examination of a biopsied material.
- (D) Three patients who underwent total or subtotal gastrectomy for the removal of the cancer. One of these three patients is included in Group C.

RESULTS

A. THE ABSORPTION OF GLYCINE FROM THE GASTRO-INTESTINAL TRACT OF PATIENTS WITH NEOPLASTIC LESIONS OF THE EXTREMITIES

Of the six patient with tumors of the extremities who were studied as control subjects, in five the peak of the plasma amino-acid nitrogen curve occurred during the first hour after ingestion of the glycine (Table I)

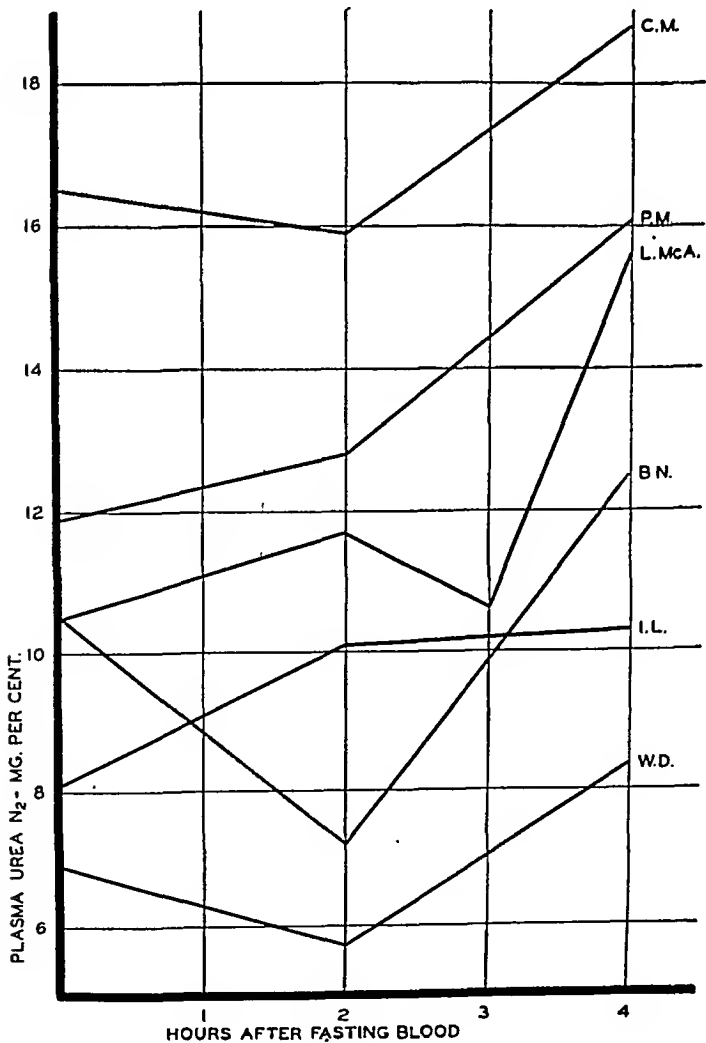
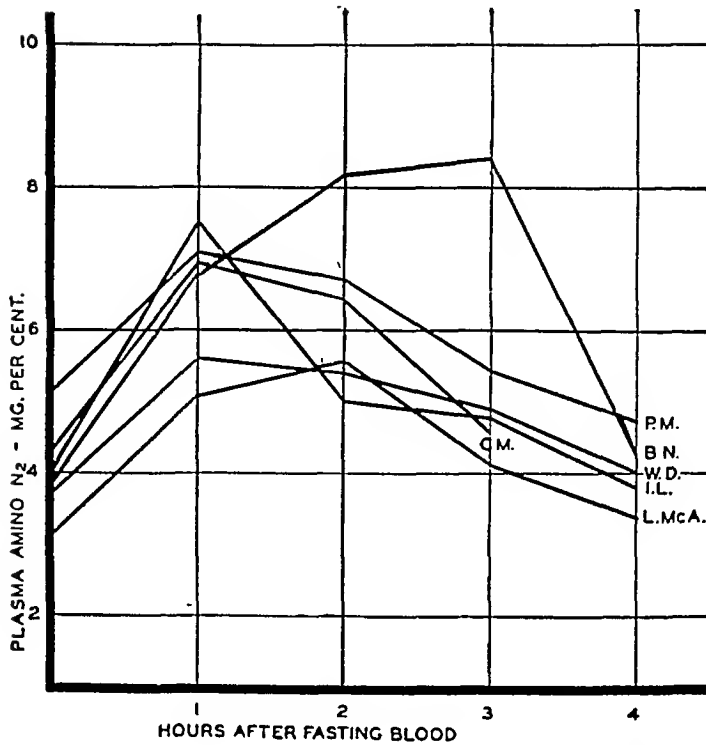
TABLE I
COMPARISON OF THE AMINO-ACID NITROGEN AND UREA NITROGEN LEVELS IN THE PLASMA OF THE PATIENTS STUDIED AFTER THE INGESTION OF 25 GM. OF GLYCINE

Patients with neoplastic lesions of the extremities.....	Duration of Time for Peak in Plasma Amino-Acid Nitrogen to Occur Hours	Height of Peak Above Fasting Plasma Amino-Acid Nitrogen Level Range Average Mg. per 100 Ml.		Type of Curve	Increase in Plasma Urea Nitrogen 4 Hours After Glycine Ingestion Range Average Mg. per cent	
Patients with gastric cancer.....	1	1.8-4.3	2.58	Slow drop of peak	1.5-5.1	3.0
Patients with noncancerous lesions of the stomach.....	2	4.1-8.8	6.61	Sharp drop of peak	1.8-5.3	3.4
Patients subjected to gastrectomy	1	3.8-5.5	4.53	Slow drop of peak	1.6-8.2	5.3
	1	3.2-9.2	5.80	Sharp drop of peak	5.0-17.5	8.75

(Fig. I). In the exception (a vegetarian of 20 years duration), the peak of absorption occurred during the third hour. The average maximum increase of the level of amino-acid nitrogen in the plasma of these six patients was 2.58 mg. per cent nitrogen, and the range of increase was from 1.8 to 4.3 mg. per cent. These values are somewhat lower than the average value of 5.8 mg. per cent obtained for four normal individuals by Kirk.⁷

There is no apparent relationship between the levels of plasma amino-acid nitrogen and those of urea (Fig. I). The average maximum increase of urea nitrogen was 3.0 mg. per cent, and the range of increase from 1.5 to 5.1 mg. per cent.

The urinary excretion of amino-acid nitrogen was measured in two of the six control subjects both for the day before and the two days after the administration of glycine (Table II). In these individuals an increased



METABOLISM IN GASTRIC CANCER

TABLE II
URINARY EXCRETION OF AMINO-ACID NITROGEN FOLLOWING THE INGESTION OF 25 GM. GLYCINE

Patient	Diagnosis	24 Hours Before Glycine Ingestion	24 Hours After Glycine Ingestion	24th to 48th Hours After Glycine Ingestion
Group A:				
L. M.	Sarcoma of thigh.....	172		
I. L.	Sarcoma of thigh.....	67	295	75
Group B:				
E. V.	Cancer of stomach.....	63	142	79
M. K.	Cancer of stomach.....	55	184	
J. M.	Cancer of esophagus.....	82	97	44
I. Z.	Cancer of stomach.....	237	172	360
Group C:				
R. G.	Peptic ulcer.....	31.0	451	104
G. F.	Gastritis.....	57.6	34.4	233
			66.0	49.8

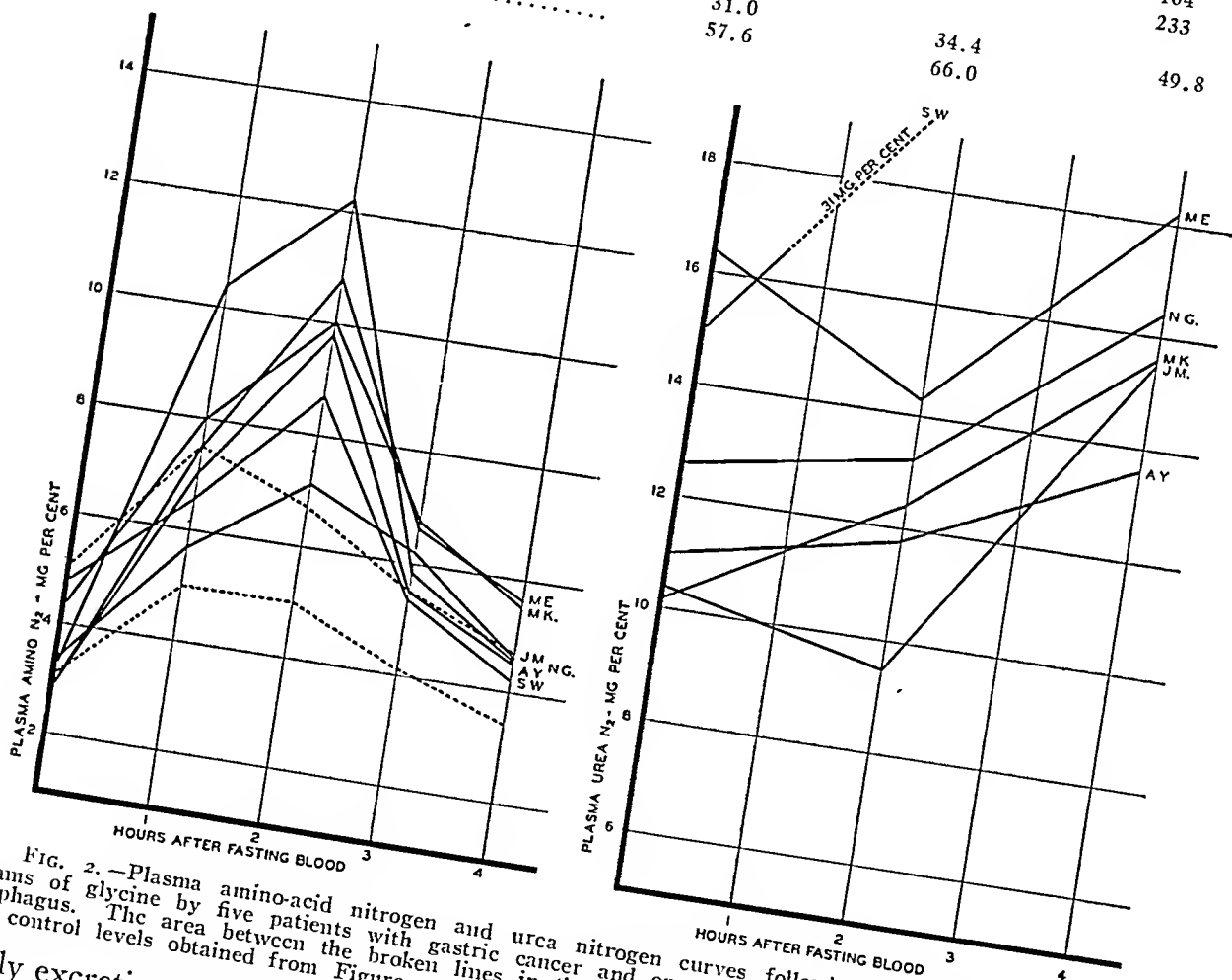


FIG. 2.—Plasma amino-acid nitrogen and urea nitrogen curves following the ingestion of 25 grams of glycine by five patients with gastric cancer and one patient with carcinoma of terminal esophagus. The area between the broken lines in the plasma amino-acid nitrogen chart represents the control levels obtained from Figure 1.

daily excretion of only 75 and 123 mg. of amino-acid nitrogen was noted after the glycine ingestion. It is interesting to note that these increased outputs represent less than one per cent of the glycine given. This observation would indicate that almost all the glycine administered was used for metabolic purposes.

B. THE ABSORPTION OF GLYCINE FROM THE GASTRO-INTESTINAL TRACT OF PATIENTS WITH GASTRO-INTESTINAL CANCER

In contrast to the findings noted in the previous group of patients, the

* FIG. 1.—Plasma amino-acid nitrogen and urea nitrogen curves following the ingestion of 25 grams of glycine by six patients with neoplastic lesions of the extremities.

peak of amino-acid nitrogen levels in the plasma of patients with gastro-intestinal cancer after the administration of glycine always occurred in the second hour. Moreover, in this group of patients the increase in the peak of the plasma amino-acid nitrogen, after the glycine ingestion of 25 Gm., was considerably higher than that observed in the previous group. The average increase was 6.61 mg. per cent, and varied from 4.1 to 8.8 mg. per cent. Thus, the average increase in the plasma of patients with gastric cancer was 256 per cent above the peak in the plasma of the control group.

The average increase of urea nitrogen in the plasma of these patients after the ingestion of glycine was found to be 5.8 mg. per cent, and the range of increase from 1.8 to 16.0 mg. per cent.

In four instance the daily urinary output of amino-acid nitrogen was measured and was found to increase for the 24 hours after administration of glycine only by from 42 to 215 mg.

Thus, it would appear that the absorption of glycine from the gastro-intestinal tract of patients bearing esophageal or gastric cancer is somewhat delayed.

C. THE ABSORPTION OF GLYCINE FROM THE GASTRO-INTESTINAL TRACT OF PATIENTS WITH BENIGN LESIONS OF THE STOMACH

To ascertain whether or not the delayed absorption of glycine by patients with gastro-intestinal cancer was due to the presence of gastric lesions and possibly to the consequent impaired gastro-intestinal motility, three patients with benign gastric disorders were studied. In these, as in the control Group A, the peak of glycine absorption occurred during the first hour. The average maximum increase of the plasma amino-acid nitrogen level was 4.53 mg., and the range of maximum increase from 3.8 to 5.5 mg. per cent. In one instance (R. G.), following a sharp drop in the plasma level of amino-acid nitrogen during the second hour, a secondary higher peak occurred. The reason for this second rise is not known, although others⁷ have demonstrated a secondary third-hour peak in the curve of some normal individuals.

The maximum increase of the plasma urea nitrogen in these patients varied from 1.6 to 8.2 mg., and the average was 5.3 mg. per cent.

The daily excretion of amino-acid nitrogen was measured in the urine of two of the three individuals and was found to increase only by 9 and 18 mg.

D. THE ABSORPTION OF GLYCINE FROM THE GASTRO-INTESTINAL TRACT OF PATIENTS WHO UNDERWENT GASTRIC RESECTION

Two of the three patients in this group previously were studied before surgical removal of their stomachs. In J. M., the patient with cancer of the terminal esophagus who was presented in Group B, the peak of glycine absorption now was reached during the first instead of the second post-

METABOLISM IN GASTRIC CANCER

absorptive hour. The height of the peak was 3.3 mg. per cent—a value somewhat lower than that noted under similar circumstances before his gastric resection (4.3 mg per cent).

In J. R., a patient who suffered from Boeck's sarcoid of the stomach and who underwent gastric resection, the peak of glycine absorption occurred in the first hour. Whereas, before surgical removal of the cancer, a lag was noted in the fall of the plasma amino-acid nitrogen level after glycine ingestion, when the stomach was resected, this "post-peak" fall was precipitous. During the test made in the preoperative period, the plasma amino-acid nitrogen increased by 3.9 mg. per cent; after the subtotal resection, the level increased by 7.1 mg. per cent.

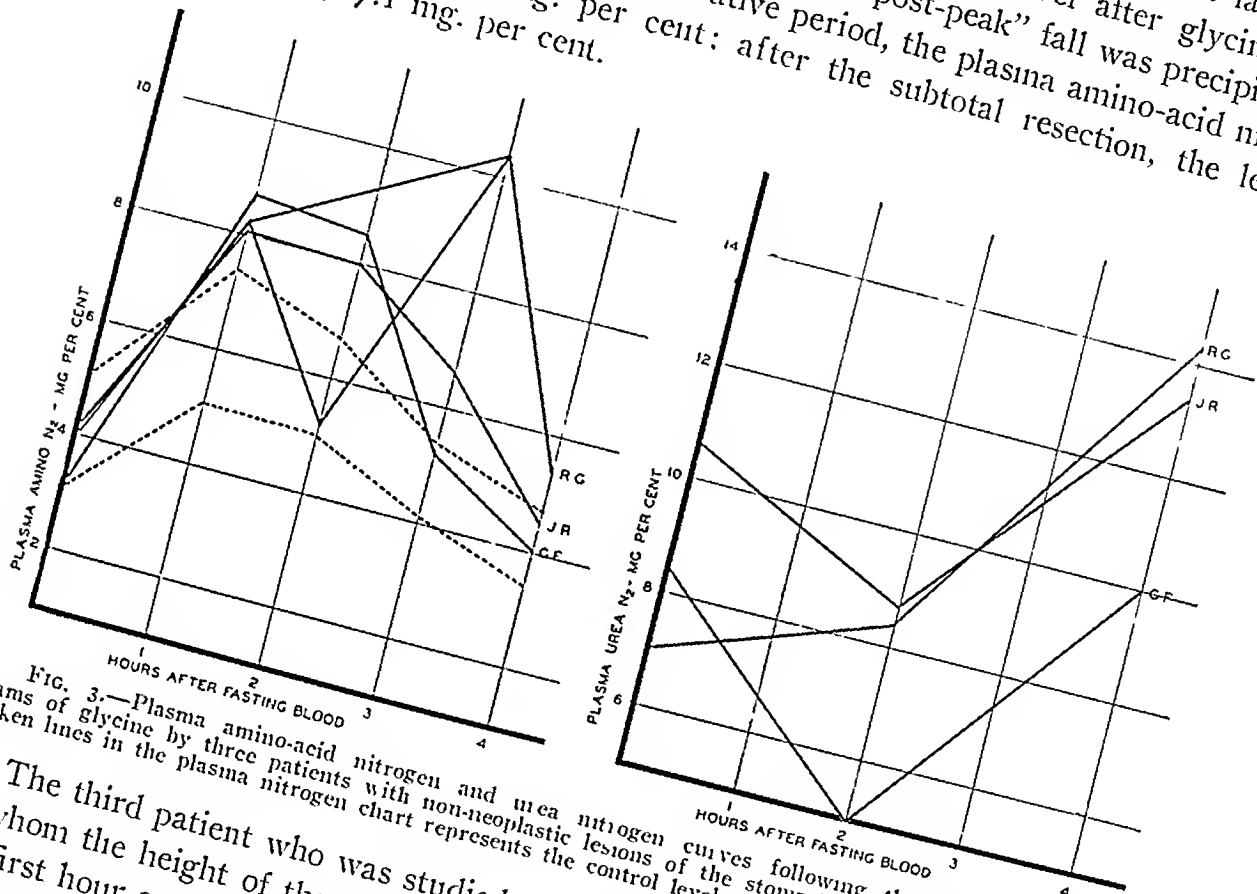


FIG. 3.—Plasma amino-acid nitrogen and urea nitrogen curves following the ingestion of 25 grams of glycine by three patients with non-neoplastic lesions of the stomach. The area between the broken lines in the plasma nitrogen chart represents the control levels obtained from Figure 1.

The third patient who was studied following total gastrectomy was F. B., in whom the height of the plasma amino-acid nitrogen level occurred during the first hour and increased by 9.2 mg. per cent. No measurements of amino-acid nitrogen excretion were made in these individuals.

In two of the three patients, a steady increase in the plasma urea nitrogen levels was noted after glycine administration. Thus, it would appear that patients who lack a large part or all of their stomach absorb orally administered glycine at a normal rate; furthermore, the abnormal delay of amino-acid nitrogen absorption from the intestinal tract of a patient with gastric cancer was corrected when his stomach was resected.

Discussion.—From the results obtained by means of the glycine tolerance test it appears that the absorption, and possibly the metabolism, of glycine by patients with gastric carcinoma is abnormal. Normally, the peak of the plasma amino-acid nitrogen curve occurs within one hour after the ingestion

of the glycine.^{4, 7} In all the controls of the present study, with but one exception, the peak did occur within one hour. In the six patients bearing gastric cancer the peak of the amino-acid nitrogen curve occurred in the second hour. This delayed peak may be due to the presence of the neoplasm which (1) alters gastro-intestinal motility and thereby mechanically hinders amino-acid absorption; or which (2) induces a metabolic disturbance through which an abnormal amino-acid absorption results. A similar metabolic abnormality has been described in patients with sprue.⁴ Moreover, the presence of marked gastric pathology (multiple peptic ulcers, diffuse Boeck's

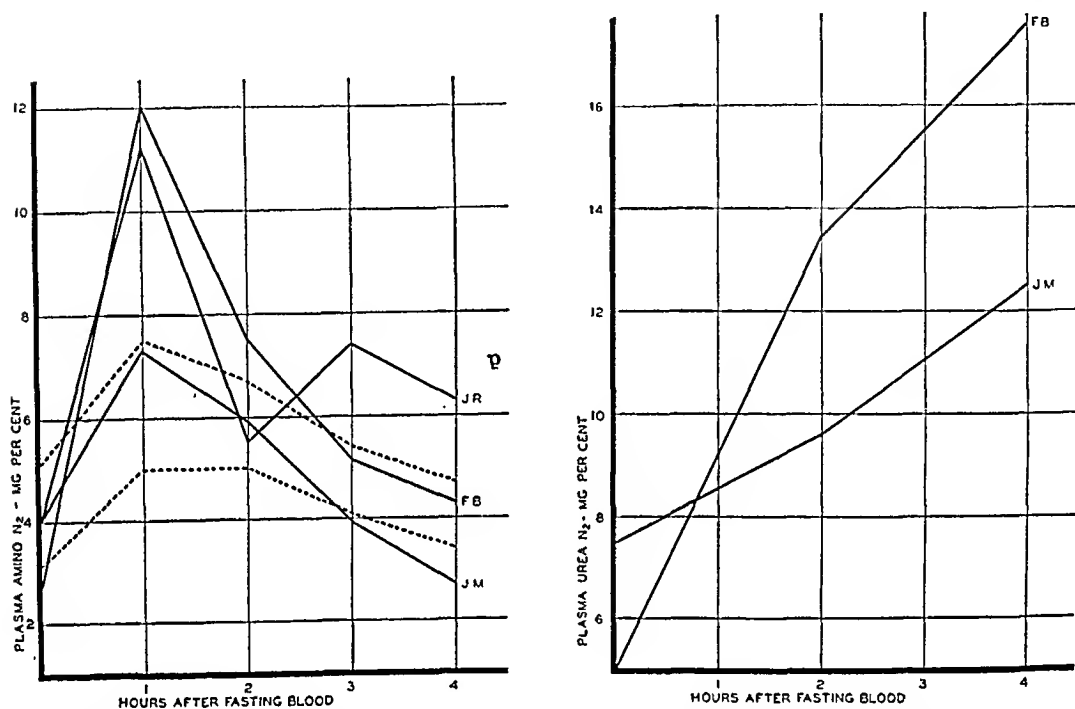


FIG. 4.—Plasma amino-acid nitrogen and urea nitrogen curves following the ingestion of 25 grams of glycine by three patients following gastrectomy. The area between the broken lines in the plasma nitrogen chart represents the control levels obtained from Figure 1.

sacoid, polypi (with follicular hyperplasia) does not appear to affect the rate of absorption of glycine from the gastro-intestinal tract.

Furthermore, after glycine ingestion the average maximum increase of the amino-acid nitrogen level (6.61 mg. per cent) in the plasma of the patients with gastric cancer, although delayed, is significantly higher than that (2.58 mg. per cent) of the six control subjects. Of the six patients with gastric cancer, five had peaks of glycine absorption higher than that of the highest control value. It has been demonstrated that the height of the plasma amino-acid nitrogen which occurs after the ingestion of glycine reflects the ability of the body to *utilize* the compound.⁷ Hence, the abnormally high peak of the amino-acid nitrogen level in the plasma of patients with gastro-intestinal cancer after the glycine ingestion suggests that these individuals have not only a slow absorption of glycine but also an impaired ability to utilize that compound at a proper rate. These suggestions ap-

METABOLISM IN GASTRIC CANCER

parently are borne out further by the observations that neither the delayed absorption nor decreased rate of utilization of the glycine by patients with gastro-intestinal cancer could be attributed to any abnormal rate of its urinary excretion. Furthermore, the *fasting* levels of amino-acid nitrogen in the plasma of these patients were within normal limits which, therefore, would indicate that the abnormalities observed were not due to the fact that the tissues of the patients were saturated with amino-acids.⁸

In summary, then, the abnormal rate of absorption and defective rate of utilization of amino-acids (glycine) by patients with gastric cancer may contribute to the high incidence of hypoproteinemia observed in these patients¹ since the production of plasma protein depends upon proper absorption and metabolism of the intermediary products of protein metabolism.

CONCLUSIONS

1. In six patients with gastro-intestinal cancer, a delayed absorption of glycine followed the ingestion of 25 Gm. of that amino-acid. This abnormality probably was due to the presence of the cancer.
2. The high peaks of plasma amino-acid nitrogen curves obtained in the patients with gastric cancer suggest a delayed rate of utilization of that compound.
3. Following removal of the stomach from a patient with gastro-intestinal cancer, a rapid, high peak of the plasma amino-acid curve was obtained. This may indicate that the presence of the carcinoma contributes to the slow absorption, but not to the impaired utilization of glycine.
4. The defective absorption and metabolism of the end-product of protein digestion in patients with gastric cancer may contribute to the hypoproteinemia state so frequently exhibited by these patients.

REFERENCES

- ¹ Ariel, I. M., Rekes, P. E., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Gastro-Intestinal Cancer X. Abnormalities of Protein Metabolism in Patients with Gastric Cancer. To be published.
- ² Ariel, I. M., Abels, J. C., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Gastro-Intestinal Cancer. XI. Nitrogen Balance Studies in Patients Undergoing Abdominal Surgery and the Incidence of Postoperative Hypoproteinemia in Patients with Gastric Cancer. To be published.
- ³ Strauss, M. B.: The Rôle of the Gastro-intestinal Tract in Conditioning Deficiency Disease. *J. A. M. A.*, 104, 613-618, 1935.
- ⁴ Erf, L. A., and Rhoads, C. P.: The Glycine Tolerance Test in Sprue and Pernicious Anemia. *J. Clin. Investigation*, 19, 409-421, 1940.
- ⁵ Van Slyke, D. D., Dillon, R. T., MacFadyen, D. A., and Hamilton, P.: Gasometric Determination of Carboxyl Groups in Free Amino-Acids. *J. Biol. Chem.*, 141, 627-669, 1941.
- ⁶ Van Slyke, D. D.: Determination of Urea by Gasometric Measurements of Carbon Dioxide Formed by Action of Urease. *J. Biol. Chem.*, 73, 695-723, 1927.
- ⁷ Kirk, E.: The Ability of Nephritic Patients to Deaminize and Form Urea from Ingested Glycine. *J. Clin. Investigation*, 14, 136-141, 1935.
- ⁸ Unpublished data, this laboratory.

THE TREATMENT OF POSTOPERATIVE HYPOPROTEINEMIA IN PATIENTS WITH CANCER OF THE COLON AND RECTUM*

GEORGE E. BINKLEY, M. B. (Tor.), JULES C. ABELS, M.D.,†

AND

C. P. RHOADS, M.D.

NEW YORK, N. Y.

FROM THE COLON AND RECTUM SERVICE OF MEMORIAL HOSPITAL, NEW YORK, N. Y.

THE PHYSIOLOGIC DERANGEMENT of patients with cancer of the colon and the rectum deserves careful consideration when surgery is contemplated. The ability of these patients to maintain normal levels of serum protein and a satisfactory status of liver function before and after operation are important factors in the successful treatment of their disease. There is considerable evidence to show that a persistent hypoproteinemia may result in tissue edema, ascites, altered motility of the gastro-intestinal tract, wound disruptions, and an increased susceptibility to infection.¹ The many complications that may follow major surgery in patients with liver disease is common clinical knowledge. These range from febrile reaction to sudden death from so-called liver shock.² Experience in our clinic has proven that many of these complications can be avoided when the patient maintains a satisfactory level of serum protein. Moreover, we feel that during the past few years, since this factor of hypoproteinemia has been given careful attention, the postoperative mortality and morbidity have been decreased (Table I).

TABLE I
OPERATIONS WITH OPERATIVE MORTALITY ON THE COLON AND RECTUM SERVICE—YEAR 1942

Type of Operation	Number of Patients	Deaths
-------------------	--------------------	--------

Rectum:

Abdomino-perineal (one stage)	55	0
Perineal Resection:		
With abdominal colostomy 8		
With perineal colostomy 2	10	0
Colostomies	54	6

Colon:

Iliotransversecolostomy	4	0
Resection of right colon	3	0
Resection of left colon (Mikulicz)	8	0
Resection of transverse colon (Mikulicz)	1	0
Exploratory for carcinomatosis	2	1
Cecostomy	1	1

Previous investigations in this hospital of a group of patients with cancer of the esophagus, stomach, colon and rectum revealed that 58 per cent in this group were hypoproteinemic.³ Also, in a study of 100 patients with gastric cancer, hypoproteinemia was found preoperatively in 67 per cent.¹ In the

* This investigation was undertaken with the aid of a grant from the National Cancer Institute.

† Finney-Howell Fellow.

POSTOPERATIVE HYPOPROTEINEMIA

latter group the hypoproteinemia was due chiefly to an inability of the livers of these individuals to fabricate albumins rather than to a deficiency of protein in the diet or to an increased protein catabolism.⁵

In the present communication an analysis of a group of patients with malignant neoplasms of the colon and the rectum is presented. An effort was made to determine in these patients the frequency and degree of hypoproteinemia before and after they were subjected to operation, and to suggest a type of treatment which was found to be satisfactory for this disorder.

In all, 65 patients were studied. These were selected from 100 consecutive admissions to the Rectum and Colon Service. The diagnosis was discarded because of inadequate studies and reports. The remaining 35 were proven in all instances. The tumors were located as follows: Ten in the right colon, 14 in the left colon, and 41 in the rectum or rectosigmoid. All patients were submitted to and survived operation. The procedure consisted of radical resection of the tumor in the patients considered operable, and a short-circuiting, palliative procedure in those who had reached the inoperable stage.

Determination of the serum protein was made by the falling-drop method of Weech, *et al.*⁶ Levels below 6.5 grams per cent were considered abnormal.^{4, 7}

In the 65 patients, hypoproteinemia was noted preoperatively in 23, or 36 per cent. This figure is lower than that found in the patients with gastrointestinal cancer³ and also lower than that in patients with gastric cancer.⁴ Apparently, the incidence and severity of the hypoproteinemia in these individuals could not be correlated with their ingestion of protein. Sixty of the 65 patients were considered to have ingested normal diets until the time of admission (Table II).

TABLE II
THE PREOPERATIVE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON

Serum Protein, Gm. per 100 ML.	No. of Patients Preoperatively	No. of Patients on Adequate Diets	No. of Patients on Inadequate Diets or who Suffered from Diarrhea
4.6—5.0	0	0	0
5.1—5.5	3	2	1
5.6—6.0	3	3	0
6.1—6.5	17	14	3
6.6—7.0	21	18	3
7.1—7.5	18	15	3
7.6—8.0	3	3	0

It is very important to note that after operation almost all the patients with cancer of the rectum and colon became hypoproteinemic. In the first postoperative week 56 of the 65 patients (86 per cent) had abnormally low levels. Preoperative, none of these patients had concentrations of less than 5.1 grams per cent, but after operation four had these very low levels. Likewise, only three had preoperatively concentrations of from 5.1 to 5.5 grams per cent, but after operation 21 had levels in this range (Table III).

TABLE III

THE PRE- AND POSTOPERATIVE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON

Serum Protein, Gm. per 100 Ml.	No. of Patients Preoperatively	No. of Patients Postoperatively
4.6—5.0	0	4
5.1—5.5	3	21
5.6—6.0	3	21
6.1—6.5	17	10
6.6—7.0	21	6
7.1—7.5	18	2
7.6—8.0	3	1

Fifty-two of the 65 patients studied received parenteral protein therapy. Apparently, a normal level of protein cannot always be obtained and maintained by dietary nitrogen nor even by the intravenous administration of from 20 to 60 grams of amino-acids (Table IV). It has been found necessary for this purpose to use blood, plasma, and a high protein-carbohydrate diet. Whole blood was employed in most instances, since its administration

TABLE IV

THE LEVELS OF SERUM PROTEIN IN PATIENTS WITH CANCER OF THE RECTUM AND COLON, WHO RECEIVED NO PARENTERAL PROTEIN POSTOPERATIVELY

Patient	Serum Protein, Gm. per 100 Ml.		Amount and Source of Nitrogen Postoperatively	Days of Nitrogen Source Administration	Serum Protein Level after Nitrogen Administration Gm. per 100 Ml.	Surgical Complication
	Preoperatively	1st Day Postoperatively				
F.G.	6.2	5.4	Intravenous amino-acids, 15-60 Gm., q.d.	10	5.5	Ileus
A.E.	6.4	6.0	Oral protein, 40 Gm., q.d.	5	5.5	
L.G.	6.7	6.2	Oral protein,	8	5.9	
E.K.	6.5	5.9	Intravenous amino-acids, 15-40 Gm., q.d.	7	6.0	
			Oral protein, 45-70 Gm., q.d.			
K.D.	6.4	5.3	Intravenous amino-acids, 30-75 Gm., q.d.	10	5.4	Marked abdominal distention
I.C.	—	5.4	Oral protein, 40 Gm., q.d.	12	5.6	Wound disruption
B.C.	6.4	5.9	Oral protein, 30-60 Gm., q.d.	14	5.9	
K.P.	6.6	—	Oral protein, 45 Gm., q.d.	18	5.7	Wound disruption

not only increases the level of serum protein but also the red count and the hemoglobin content. Infusions of blood plasma were given to those patients who had hypoproteinemia unassociated with anemia. As soon as the patients could tolerate food after operation, high protein diets were used in all instances. Milk protein was given from the third or fourth post-operative day and the amount increased until the patients received about 100 grams daily. Thirty-two patients received only blood transfusions, while 20 received both whole blood and plasma. By these measures it was possible

POSTOPERATIVE HYPOPROTEINEMIA

to raise the concentrations of serum protein in 46 of the 52 patients. These increases ranged from 0.2 to 2.1 grams per cent, and the average increase was 1.6 grams per cent. All the levels finally were above 5.0 grams per cent (Table V). Fifty of the 52 patients (96 per cent) were hypoproteinemic after operation, but after the treatment described only 24, or 46 per cent, had serum protein levels below normal.

TABLE V
THE SERUM PROTEIN LEVELS, IN PATIENTS WITH CANCER OF THE RECTUM AND COLON, PREOPERATIVELY, POSTOPERATIVELY, AND AFTER THERAPY

Serum Protein, Gm. per 100 Ml.	Number of Patients		
	Preoperatively	Postoperatively	After Therapy
4.6—5.0	0	4	0
5.1—5.5	2	20	3
5.6—6.0	3	17	5
6.1—6.5	13	9	16
6.6—7.0	19	2	20
7.1—7.5	13	0	6
7.6—8.0	1	0	2

Although it is essential to combat immediately the hypoproteinemia in patients subjected to surgery by the repeated administration of blood or plasma, it would not be possible to continue such procedures indefinitely. However, if the hypoproteinemia which developed after surgical manipulation was only a transitory affair, then the temporary replacement of serum protein by infusion would be feasible until that time when the patient would fabricate sufficient protein from dietary nitrogen. In order to ascertain whether or not patients with cancer of the colon and rectum eventually could depend only upon dietary nitrogen to maintain their preoperative or normal concentrations of serum protein, determinations of that substance were made in a group of 14 patients at variable periods after they had received their last infusion of blood or plasma (Table VI). With but one exception, it was found that the serum protein levels of these individuals,

TABLE VI
THE ABILITY OF PATIENTS WITH CANCER OF THE RECTUM AND COLON TO FABRICATE PROTEIN AFTER OPERATION

Patient	Serum Protein, Gm. per 100 Ml.			
	Preoperative Level	Level During First Week Postoperative	Days After Last Infusion	Level At That Time
A.W.	6.8			
H.R.	7.8	5.7	60	7.5
J.C.	6.6	6.4	20	6.8
A.R.	6.6	5.2	34	7.5
J.F.	7.6	5.7	150	7.0
C.C.	5.3	5.4	100	6.6
J.D.	7.1	4.8	30	6.3
J.R.	6.7	6.6	84	6.3
K.D.	6.4	5.0	23	6.6
E.S.	7.0	6.2	55	6.4
A.E.	6.4	5.5	20	6.4
L.C.	7.5	5.7	22	6.8
C.D.	7.1	5.3	20	7.1
A.M.	6.8	6.1	31	7.0
				6.9

from 20 to 150 days after they received their last parenteral protein, were significantly higher than the levels during the first postoperative week. Of the 14 patients, one had hypoproteinemia preoperatively; during the first postoperative week this abnormality was noted in 13; and, finally, considerably after the last parenteral protein, only four still had mild reductions of their serum protein concentrations. These observations would indicate, therefore, that the chief purpose of the measures taken in this investigation to combat postoperative hypoproteinemia was to supply enough protein during that short period when the surgical procedure might have increased protein catabolism or impaired protein fabrication.

The ability to counteract hypoproteinemia was greatly handicapped by the presence of acute infections. Of the 52 patients studied, in which the above form of treatment was instituted, six failed to obtain any increase in the serum protein level; and four of these six suffered with an acute infection. In these instances, the refractory hypoproteinemia might have been due to the effects of the infection on the liver or to additional protein catabolism. Other workers⁸ have demonstrated the presence of impaired hepatic function during pneumonia, sepsis, and acute rheumatic fever.

Eighteen of the 52 patients studied had infections of the genito-urinary tract for which sulphone drugs were employed. It was noted that the amount of blood and plasma required to combat the hypoproteinemia of these individuals was greater than that needed for the patients without infections. The former group received from 500 to 3150 ml. of blood, the average being 1800 ml., while the average amount of blood required for the latter group with hypoproteinemia ranged from 250 to 2700 ml. and averaged 950 ml. The average amount of plasma was 1200 ml. for the patients with infections, and 740 ml. for those who did not develop infections. Of the 18 patients with bladder infections, four, or 23 per cent, failed to show any rise in their levels of serum protein during the first 14 days of treatment. In ten other instances, or 55 per cent, an increase of the serum protein level was noted only after the 14th day of treatment (Table VII).

TABLE VII
THE ABILITY OF INFECTION TO IMPAIR THE EFFECTS OF HIGH PROTEIN THERAPY

	Patients without Infection of the Bladder	Patients with Infection of the Bladder
Number	34	18
No serum protein rise after therapy in	6%	23%
Delayed serum protein rise (14 days or more) in. . .	29%	55%

These findings strongly suggest that the treatment of hypoproteinemia is made much more difficult by the presence of infection, which seems to set up a vicious circle in that it induces a fall in the serum protein level, and the presence of hypoproteinemia decreases the patient's resistance.¹ In certain of these individuals with infection it may be difficult or impossible to maintain a satisfactory serum protein concentration; nevertheless, the administration of blood or plasma in these instances probably avoids the

POSTOPERATIVE HYPOPROTEINEMIA

development of dangerously low serum protein levels and consequent grave surgical complications.

CONCLUSIONS

1. The incidence of hypoproteinemia in patients with cancer of the rectum and colon was found to be 36 per cent. This incidence is increased to 86 per cent after the patients have been subjected to surgical procedure.
2. In the early preoperative period, hypoproteinemia is best treated by intravenous plasma protein. Later in the convalescence, sufficient amounts of dietary nitrogen may be ingested to counteract the postoperative hypoproteinemia.
3. It is believed that the correction of the postoperative hypoproteinemia is, in great part, responsible for the decreased mortality among patients with rectal and colon cancer.
4. The presence of infection in the patients studied considerably impairs the effectiveness of the measures outlined to combat the hypoproteinemia.

REFERENCES

- ¹ Whipple, G. W.: Hemoglobin and Plasma Protein: Their Production, Utilization, and Interrelation. *Am. J. Med. Sc.*, 203, 447-489, 1942.
- ² Heyd, C. G.: Mortality Factors in 4000 Operations on the Biliary System. *Mississippi Doctor*, 18, 117-123, 1940.
- ³ Abels, J. C., Rekers, P. E., Binkley, G. E., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Gastro-Intestinal Cancer. II. Hepatic Dysfunction. *Ann. Int. Med.*, 16, 221-240, 1942.
- ⁴ Ariel, I. M., Rekers, P. E., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Gastro-Intestinal Cancer. X. Abnormalities of Protein Metabolism in Patients with Gastric Cancer: To be published.
- ⁵ Ariel, I. M., Abels, J. C., Pack, G. T., and Rhoads, C. P.: Metabolic Studies in Patients with Gastro-Intestinal Cancer. XI. The Postoperative Hypoproteinemia in Patients with Gastric Cancer: To be published.
- ⁶ Weech, A. A., Reves, E. B., and Goettsch, E.: The Relationship Between the Specific Gravity and Protein Content in Plasma, Serum, and Transudate from Dogs. *Jour. Biol. Chem.*, 113, 167-174, 1936.
- ⁷ Hill, R. H., and Trevorrow, V.: Plasma Albumin, Globulin and Fibrinogen in Healthy Individuals from Birth to Adult Life. *J. Lab. and Clin. Med.*, 26, 1838-1849, 1941.
- ⁸ Paulson, M., and Wyler, C. I.: Multiple Tests in Gastro-enteric Malignancy: The Value of Bromosulfalein, Hippuric Acid, and van den Bergh Reaction in Detecting Hepatic Metastases with Evaluation of Normality of Hippuric Acid Test. *Ann. Int. Med.*, 16, 872-878, 1942.

ACCESSORY SPLEEN IN THE SCROTUM

REVIEW OF LITERATURE ON ECTOPIC SPLEENS AND THEIR ASSOCIATED SURGICAL SIGNIFICANCE

J. M. EMMETT, M.D., AND M. L. DREYFUSS, M.D.

CLIFTON FORGE, VA.

FROM THE DEPARTMENTS OF SURGERY AND PATHOLOGY, CHESAPEAKE AND OHIO HOSPITAL, CLIFTON FORGE, VA.

THE PRESENCE of an ectopic spleen in the scrotum, simulating a testicular tumor, is a rare enough finding to warrant recording.

Case Report.—A white male, age 47, was admitted to the Surgical Service of the Chesapeake and Ohio Hospital on March 3, 1942.

About seven months previously, he had noticed, for the first time, a small lump in the right groin. It did not give him discomfort, but he was advised that he had a hernia which should be repaired.

He was known to have a diverticulosis of the colon which caused frequent attacks of abdominal pain. Otherwise, his family and personal history were irrelevant.

Both inguinal rings were patulous and a definite hernial sac protruded on the right side. A smooth, round, nontender, firm mass was found attached to the upper pole of the left testicle. It was about half as large as the testicle, which seemed normal in size and consistency. This swelling had never been noticed by the patient. *Pre-operative Diagnosis:* Indirect inguinal hernia, bilateral. Tumor of left testicle.

Operation.—The right inguinal hernia was repaired; and the left scrotum was incised and the testicle delivered. The tumor was found to be attached, by a broad base, to the tunica albuginea at the upper pole close to the head of the epididymis. It was encapsulated and did not penetrate into the testicle. It was removed by sharp dissection. The testicle, the epididymis and the spermatic cord appeared normal.

Pathologic Examination.—The specimen was almost completely covered with a dense, pearly-grey, glistening capsule. It measured $4 \times 3.5 \times 2$ cm. It was firm and elastic. The cut sections showed brownish-red tissue, with an irregular network of greyish, fine trabeculae. The microscopic sections showed normal splenic tissue, with rather small follicles, and hyperplastic red pulp. The sinuses were almost bloodless and collapsed (Fig. 1).

The patient made an uneventful recovery and was discharged three weeks after operation.

COMMENT.—Puzzling as such a location of an ectopic spleen may appear on first sight, it will be readily understood if one considers the close topographic relation between spleen and urogenital organs during early intra-uterine life. The differentiation of the spleen begins in about the fourth to fifth week. It is completed in the twelfth week. During this time, the spleen is transformed from a trilobated into a single organ. It is situated between the mesonephric and the urogenital fold. The mesonephros (wolffian body) reaches its maximal cephalad extension at the time when the spleen begins to develop. The caudal migration of the genital gland begins in the eighth to tenth week. Therefore, we must place the teratogenetic period, during which portions of the spleen are transported downwards with the genital gland, between the fourth and tenth week; most probably in the sixth

ECTOPIC SPLEENS

to eighth week (Putschar²⁰) because during this time the splenic tissue is already well developed and is still in close contact with the wolffian body. Splenic tissue then accompanies the genital gland in its descensus and is finally found in the scrotum in close association with the upper pole of the left testicle and the epididymis or, in the female, in the region of the mesosalpinx and the mesovarium. The path of this migration is, in some cases, visibly demonstrated by a band of tissue—consisting of fibrous and/or splenic tissue—which connects the normally located spleen with the ectopic spleen in the scrotum or the broad ligament. This band runs from the splenic hilus anteriorly to the intestines and ends near the testicle or the mesosalpinx. A nodule of splenic tissue has been seen, in some cases, at the distal end (Fig. 2). Putschar²⁰ has collected several cases with such bands between the spleen and genital organs. Since then, another such case has been published by Fischer and Gissel⁷:

Case of Fischer and Gissel.⁷—The patient was a 13-year-old boy who was operated upon for an undescended testicle in the left inguinal canal. A flat, further upward, round band extended from the epididymis into the left side of the abdominal cavity. It was followed for 20 cm. It was as thick as a knitting needle, smooth and dark red. The lowermost 8 cm. were removed and found to consist of typical splenic tissue.

The authors express the opinion that this malformation occurs more frequently than the recorded cases would indicate but that it is either erroneously interpreted or not published.

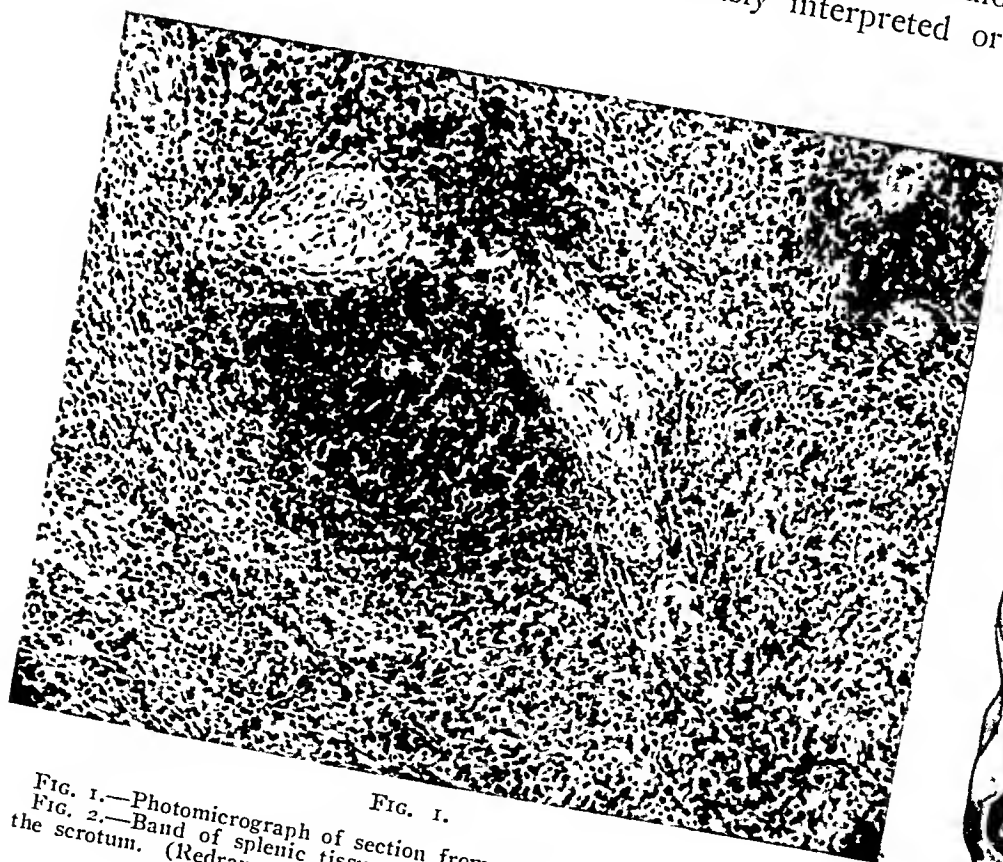


FIG. 1.

FIG. 1.—Photomicrograph of section from paratesticular tumor showing characteristic splenic tissue.
FIG. 2.—Band of splenic tissue connecting the normally located spleen, with an accessory spleen in the scrotum. (Redrawn from Sneath,²³)



FIG. 2.

The literature contains, in addition, several reports of cases in which—like in our own case—the ectopic spleen in the scrotum was not connected with the spleen.

Case of Finary.⁶—The patient was a male newborn child with a congenital left inguinal hernia. The left testicle seemed twice as large as the right and had a different shape. A dark brown and purple, round swelling at the head of the epididymis was removed. It was covered with peritoneum and consisted of splenic tissue.

Case of Talmann.²⁴—The patient, a 22-year-old soldier, had a painful swelling in his left scrotum. During malarial attacks this swelling reached the size of a goose egg. One nodule of splenic tissue, 2.5 cm. in diameter, was found at the head of the left epididymis, another, 0.4 x 0.5 x 0.8 cm., was present in the spermatic cord.

Case of Osseladore.¹⁷—The patient, a 19-year-old white boy had, since birth, three nodules in his left scrotum which had grown corresponding to the body development. The largest nodule suggested at the time of operation, as to size and consistency, a third testicle. The two smaller ones were pedunculated. All three consisted of splenic tissue which was, in places, sclerotic and contained several iron-calcium deposits.

Case of Settle.²²—The patient, an adult, suffered from a painful enlargement of the left testicle during the acute febrile phases of a tertian malaria. An enlarged accessory spleen was found in the scrotum.

Even these few cases illustrate the almost impossible task of a correct pre-operative diagnosis. Probably the true condition will only be recognized after microscopic study. However, in the presence of a long-existing tumefaction of the left testicle, particularly when accompanied by an inguinal hernia, the possibility of an ectopic spleen should be considered in the already difficult diagnosis of testicular tumors. (The painful periodic swelling associated with malarial attacks in the cases of Settle,²² and Talmann,²⁴ might perhaps have led to hazarding a tentative diagnosis).

Although it was not possible to inspect the spleen in the present case, we may conclude, from the other similar reports, that a normal spleen was present in normal location. Thus, we would list this case of scrotal spleen among the accessory aberrant) spleens. A certain confusion prevails as to the correct nomenclature of spleens in anomalous location. A clear distinction should be made between the following types: (1) Wandering spleen. (2) Double spleen. (3) Multiple spleen. (4) Accessory (aberrant) spleen. These types differ from each other in their formal genesis as well as in their clinical significance.

The wandering or floating spleen is the type most frequently involved in surgical complications. Since Abell¹ reported 95 cases of wandering spleen, with torsion of the pedicle, additional publications have brought the total to about 120. The wandering spleen may be found in any part of the abdominal cavity and—as in ventral or diaphragmatic hernia—even outside the abdomen. It is much more frequent in women than in men, and its incidence is especially high in multiparae. Only three cases have been reported in children (Truesdale and Freedman²⁶). It is, therefore, assumed that the relaxation of the abdominal wall plays an important part in the causation of the displacement, although this is probably not the only factor involved. Minor, easily overlooked disturbances of peritoneal development, and consequent faulty attachment of the organ, are most likely equally responsible. The relative frequency

ECTOPIC SPLEENS

with which wandering spleen is found in malaria, is unexplained. The weight of these spleens is far below that found in leukemia, Banti's or Gaucher's disease, and no case of wandering spleen associated with any of these conditions has been observed.

Symptoms usually are due to torsion of the vascular pedicle. The symptomatology varies according to the location of the spleen and is that of the torsion of the pedicle of an intra-abdominal tumor. Transitory attacks of colicky pain have occasionally occurred preceding the final attack.

Only in rare instances, has the wandering spleen, as such, caused complications which necessitated surgical relief or interfered, after torsion had occurred, with the function of other organs. A wandering spleen in the pelvis acting as an obstetric impediment has been described by Ottow,¹⁸ Intestinal obstruction has been reported by Mauro,¹⁵ Pacchini,¹⁹ Salvin,²¹ and Harris.¹⁰ Cases of gastric volvulus have been published by Lamarque,^{et al.,}¹³ Bertone,⁵ and Zhdanovich.²⁸ A wandering spleen was the cause of chronic dyspepsia in the case of Hjort.¹¹

Splenectomy is the only method of treatment. Conservative measures, as attempting to untwist the pedicle, are contraindicated. The results are satisfactory, although the mortality rate in pregnant women is considerable. Double spleen is exceedingly rare. In this condition, two, as to size and shape, equivalent spleens are found in place of the single organ. A discussion as to the origin of this malformation is beyond the scope of this paper. The reader is referred to the monograph of Putschar.²⁰ The literature contains no reference of double spleens of clinical significance.

We speak of multiple spleens (3-10) in the left hypochondrium or scattered over the visceral or parietal peritoneum of the entire abdominal cavity (up to 400). They may be due to faulty development of the multiple splenic anlage or to multiple autotransplants after a (intra-uterine) trauma to the spleen. Krueger and Mast,¹² and Hambrick and Bush,⁹ have recently described multiple splenic implants after splenic injury and splenectomy, and have reviewed the literature. The multiple spleens are of little clinical significance. However, Leriche and Gravier¹⁴ have reported the torsion of the pedicle in one of several multiple spleens, complicated by rupture and intra-abdominal hemorrhage, and treated by multiple splenectomy.

By far the most frequent type are the accessory (aberrant, supernumerary) spleens in the presence of a normally formed spleen in correct position. They are found in about ten per cent of all autopsies. Their number varies, and is rarely over 40. Most of them are found in the immediate neighborhood of the spleen but they are encountered also in the upper omentum, the gastroduodenal ligament, the mesocolon, and in the pancreas. Only very rarely are they seen in other intra-abdominal locations or in the scrotum. Their size varies from that of a pinhead to four centimeters in diameter. They are usually sessile but some are pedunculated. They rarely produce clinical

symptoms by torsion of the pedicle (Alexander,² and Alexander and Romanes,³ Geiger,⁸ and Settle²¹) or cause intestinal obstruction (Bainbridge,⁴ Voss,²⁷ and Temoin²⁵) or both (Settle²²). A curiosity is the case of Morris, Lederer and Fradkin.¹⁰ Their patient had his spleen removed for thrombocytopenic purpura. A walnut-sized accessory spleen was left in the abdomen. The patient was well only for a short while but then the blood dyscrasia returned due to the action of the accessory spleen. Considerations along this line would make the search for accessory spleens important, also, where splenectomy for hemolytic jaundice is performed.

SUMMARY

A case of accessory spleen in the scrotum is reported and the genesis of the malformation discussed. Similar cases in the literature are summarized. The various types of spleens in anomalous location are surveyed and their clinical importance evaluated.

BIBLIOGRAPHY

- 1 Abell, I.: Wandering Spleen with Torsion of Pedicle. *ANNALS OF SURGERY*, 98, 722-735, 1933.
- 2 Alexander, R. Ch.: Accessory Spleen with Recurring Torsion of its Pedicle. *Lancet*, 217, 17, 1929.
- 3 Alexander, R. Ch., and Romanes, A.: Accessory Spleen Causing Acute Attacks of Abdominal Pain. *Lancet*, 2, 1089-1091, 1914.
- 4 Bainbridge: Quoted by Putschar.²⁰
- 5 Bertone, C.: Occlusione e turbe funzionali dello stomaco e dell' intestino da ectopia splenica o da tumore di milza. *Riforma Medica*, 50, 765-770, 1934.
- 6 Finaly, R.: Bijmilt aan de epididymis in een aangeboren liesbruek bij een zuigling. *Nederl. Tijdschr. Geneesk.*, 2, 397-400, 1926.
- 7 Fischer, W., and H. Gissel: Ein eigentuemlicher Operationsbefund: Milzgewebstrang zum Nebenhoden ziehend. *Brun's Beitr. z. klin. Chir.*, 161, 595-598, 1935.
- 8 Geiger, Ph.: Ein Fall von stielgedrehter Nebenmilz. *Zentralbl. f. Chir.*, 58, 1772, 1931.
- 9 Hambrick, R. A., and Bush, J. D.: Autoplastic Transplantation of Splenic Tissue in Man, Following Traumatic Rupture of the Spleen. *ANNALS OF SURGERY*, 115, 84-92, 1942.
- 10 Harris, H. A. H.: Case of Wandering Spleen Causing Intestinal Obstruction. *Brit. J. Surg.*, 15, 163-165, 1927.
- 11 Hjort, E.: Wandering Spleen with Dyspeptic Symptoms. *Med. Rev. Bergen*, 53, 321-324, 1936.
- 12 Krueger, J. T., and Mast, H. E.: Splenic Transplants Following Traumatic Rupture of Spleen and Splenectomy. *Am. J. Surg.*, 58, 289-293, 1942.
- 13 Lamarque, P., Morgue-Molines, E., Betoulières, P., and Ginestie, J.: Volculus gastrique et sténose colique secondaires a une ectopie pelvienne de la rate. *Arch. d'électric. med.*, 46, 107-115, 1938.
- 14 Leriche and Gravier: Rates multiples en position droite inter-hepato duodeno-colique; volvulus d'un des pedicules: éclatement d'une des rates; hemorrhagie intraperitoneale; laparotomie; splenectomies multiples; guérison. *Lyon Chir.*, 19, 107, 1922.
- 15 Mauro, M.: Due casi di milza malarica ectopica e torta sul peduncolo complicati da occlusione intestinale meccanica. *Riforma Med.*, 50, 1153-1158, 1934.
- 16 Morrison, M., Lederer, M., and Fradkin, W. Z.: Accessory Spleens: Their Significance in Thrombocytopenic Purpura Hemorrhagica. *Am. J. Med. Sci.*, 176, 672-681, 1928.

ECTOPIC SPLEENS

- ¹⁷ Oselladore, G.: Milze succenturiate annessa al testicolo. Arch. ed atti d. Soc. Ital. di Chir., 35, 754-758, 1929.
- ¹⁸ Ottow, B.: Eine dystope im Douglas gelegene Milz als Geburtshindernis: Extirpation in der Schwangerschaft. Zentralbl. f. Gynaek., 60, 1107-1110, 1936.
- ¹⁹ Pachinni, P.: Ptosi splenica e sindrome occlusiva intestinale. Policlinico, sez. prat., 29, 905-908, 1922.
- ²⁰ Putschar, W.: Die Entwicklungsstoerungen der Milz: in H. Schwalbe's Morphologie der Missbildungen des Menschen und der Tiere. Vol. 3, 760-856, G. Fischer, Jena, 1934.
- ²¹ Salvin, A. A.: Ectopic Spleen Causing Intestinal Obstruction. ANNALS OF SURGERY, 92, 263-269, 1930.
- ²² Settle, E. B.: The Surgical Significance of Accessory Spleens. Am. J. Surg., 50, 22-26, 1940.
- ²³ Sneath, W. A.: An Apparent Third Testicle Consisting of a Scrotal Spleen. J. Anat. & Physiol., 47, 340-342, 1912-13.
- ²⁴ Talmann, J. M.: Nebenmilzen im Nebenhoden and Samenstrang. Virchow's Arch., 259, 237-243, 1926.
- ²⁵ Temoin, D.: Rate accessoire simultant au néoplasm de l'intestin. Arch. provinc. de Chir., 7, 622, 1898.
- ²⁶ Truesdale, P. E., and Freedman, D.: Wandering Spleen with Torsion of Pedicle. Surgery, 4, 700-707, 1938.
- ²⁷ Voss, P.: Accessory Spleen Associated with Chronic Intestinal Obstruction. Austral. & New Zealand J. Surg., 3, 287-288, 1934.
- ²⁸ Zhdanovich, S. N.: Volvulus of Stomach Caused by Torsion of Dislocated Spleen. Vestnik Khir., 34, 157-158, 1934.

SPONTANEOUS RUPTURE OF THE URINARY BLADDER*

REPORT OF CASE OF SECOND RUPTURE

WILLIAM BERRY MARBURY, M.D., AND LT. COMDR. WESLEY FRY, M.C.

WASHINGTON, D. C.

THERE has been considerable discussion as to what constitutes a "spontaneous" rupture of the urinary bladder. Some authors^{1, 2, 3} have preferred to designate nontraumatic ruptures as "idiopathic" when there was no apparent pathology in the bladder, and as "pathologic" when there was. Sisk and Wear⁴ attributed the confusion in terminology to the fact that the word, "spontaneous," has not been accepted in its proper sense; that is, as proceeding from an internal impulse, without external force. They contended: "If the bladder ruptures without external stimulation, it is spontaneous and deserves to be reported as such." Cases which have recently been reported as spontaneous ruptures have included both those caused by overdistention from obstruction and those caused by a pathologic condition of the bladder wall, either of primary or of secondary origin. Thus, the use of the term now seems established to include all nontraumatic ruptures of the urinary bladder.

That spontaneous rupture is a rare condition is shown by the fact that Besley⁵ found only one spontaneous rupture among 23 cases of ruptured bladder at the Cook County Hospital. Baumer⁶ listed 27 cases of non-traumatic rupture, which he had found reported in the literature during the fourteen years preceding 1913. Stone⁷ stated that up to 1931 only 40 cases had been reported. He reported two additional cases. These series do not appear to include cases of spontaneous rupture during pregnancy nor those due to an extension of a tubo-ovarian abscess. Up to 1941, 34 cases of the former had been reported and 58 of the latter condition.

As far as we have been able to determine, the following case of a second spontaneous rupture of a urinary bladder is the only one of its kind to have been reported.

Case Report.—C. M., white, male, age 37, was admitted to Emergency Hospital, March 19, 1941, complaining of pain in the abdomen. Twenty-four hours before admission he had been taken with a severe abdominal pain, which gradually increased in intensity. He had vomited twice during the 24 hours. The patient stated that for the previous week he had been drinking from one and one-half to three pints of whiskey a day. He also said that when he was age 25 he had begun drinking periodically, at intervals varying from a few months to eight months, and with drinking periods lasting from 10-14 days. In 1930 he was treated for lues and had received injections for 14 months.

The patient had had a previous admission to Emergency Hospital, November 14, 1940, because of abdominal pain and an inability to void, following a two-weeks' period

* Read before the Clinico-Pathological Society of Washington, D. C., December 1, 1942.

SPONTANEOUS RUPTURE OF BLADDER

of drinking. His spinal fluid had shown a positive Wassermann and a colloidal gold curve of 1111100000. At that time a diagnosis was made of "urinary retention of undetermined etiology; possible cord bladder."

In April, 1940, eight months prior to his first admission to Emergency Hospital, he had had a rupture of the urinary bladder, following an alcoholic debauch. He was operated upon at the West Jersey Homeopathic Hospital, and about 1,000 cc. of urine was evacuated from the abdomen. Exploration revealed that the urinary bladder was ruptured on its posterior surface, and that the posterior wall was extremely thin at several points. The bladder was drained by a large rubber tube, and two large cigarette drains were placed in the pelvis, one on each side of the bladder. A biopsy of the bladder wall showed "papillary cystitis." A blood Wassermann was negative. A roentgenogram of the chest was negative. The patient remained in the hospital for 69 days, from April 1 to June 8, 1940.

At the time of his second admission to Emergency Hospital, his temperature was 98.6°F., pulse 78, respirations 20. Upon examination, it was noted that the pupils did not react to light but that they did to accommodation. The reflexes were normal and the Babinski test was negative. There were no sensory disturbances. The chest was normal. The abdomen was somewhat distended and rigid. There was dullness in both flanks. An examination of the urine was essentially negative, except for the presence of an occasional red blood cell. An examination of the blood showed a white cell count of 17,700 of which 93 per cent were polymorphonuclears and 6 per cent lymphocytes. A spinal Wassermann was negative, and the colloidal gold curve was 0000000000. In spite of the patient's previous history, the possibility of a rupture of the bladder was not seriously considered. It was thought that he had a ruptured duodenal ulcer. Operation was advised but was refused. Permission for operation was given eight hours later.

Operation.—Under spinal anesthesia, a right rectus incision was made and a careful exploration of all the abdominal viscera undertaken. The abdominal cavity contained about 1,000 cc. of clear fluid, apparently urine, as it had an ammoniacal odor. There was a perforation in the fundus of the urinary bladder, to the left of the midline. The opening was about one centimeter in diameter, and through it a stream of urine was spouting from the bladder. There was only a moderate peritonitis present, with a number of filmy adhesions between loops of the bowel. The fluid contents of the peritoneal cavity were aspirated, and the rent in the bladder repaired with two layers of Dulox sutures. The abdomen was closed in layers, without drainage. A retention catheter was inserted into the bladder through the urethra.

During the first three of four days after the operation, the patient received oxygen nasally, fluid intravenously, and one blood transfusion. On the second postoperative day his temperature was 104.6°F., and on the eighth day it was normal. From then on he made an uneventful recovery. On the tenth postoperative day, Dr. H. N. Dormau made a cystoscopic examination and found no pathologic condition of the bladder. The patient was discharged against advice on the twelfth postoperative day. He has been seen since his discharge and was found to be in good condition.

COMMENT.—In the foregoing case, both of the ruptures were spontaneous and both involved the posterior wall of the fundus, although the second rupture was in a different location from the first one. There was no apparent pathology in the bladder wall, and no history of injury. The etiologic factors cannot be determined definitely, but it is possible that the ruptures were associated with a luetic condition and acute alcoholism. There are numerous reported cases of bladder rupture occurring during a period of alcoholism, but

in these cases the immediate cause of the rupture was traumatic, either concussion or penetrative.

The most frequent cause of spontaneous rupture is hyperdistention of the bladder wall. The overdistention arises from an obstruction to the urinary outflow, usually due to an unrelieved stricture of the urethra. Less often the obstruction is due either to pressure upon the urethra from an enlarged prostate or to a blockage of the tract by a stone. Gross retention of the urine with intramural tension may result from a neurogenic dysfunction of the bladder wall. Wilson⁸ has reported an unusual case of spontaneous rupture due to cord bladder in a patient having tabes dorsalis. His case is somewhat similar to the one being reported in that both patients had syphilis. In Wilson's case, hyperdistention was caused by syphilitic damage to the accessory tracts proximal to the column of Burdach, through which passes the afferent arm of the reflex governing the tone of the musculature and sphincter of the bladder. The consequent loss of tone of the musculature and the increased tone of the sphincter amounted to obstruction at the bladder neck. At operation, performed within a few hours after the onset of symptoms, a large hole was found in the bladder wall, permitting the introduction of three fingers into the cavity of the bladder. The defect in the bladder wall was sutured in layers. The bladder and the peritoneal cavity were drained. The patient died on the second postoperative day.

The cases of spontaneous rupture which are not caused primarily by hyperdistention usually result from morbid changes within the bladder wall. Degeneration of the musculature, appearing as areas of fibrosis or necrosis, are in some instances a secondary result of chronic distention. Baumer⁶ reported a case of a 58-year-old man who had an hypertrophied prostate and a history of early gonorrhea. At autopsy, the bladder wall showed a severe cystitis and multiple areas of necrosis in the hypertrophic musculature. Pathologic changes within the wall of the bladder may result from primary diseases of the bladder, such as carcinoma, ulceration, diverticula, tuberculosis, or syphilis. The bladder wall may also be affected by the extension of an adjacent neoplastic or inflammatory mass. A fistulous connection between the bladder and the inflammatory mass may be established, resulting in an extravasation of the urine. Stone⁷ reported such a case. A girl, nine years of age, who four years previously had had a nontuberculous osteomyelitis of the right hip, developed pain in the right hip accompanied by a rise in temperature. Three weeks later there was a sudden onset of micturition, burning, spasm, and extreme dysuria. The urine was loaded with pus. A few days later an abscess of the right hip was incised and evacuated. Ten days later the dressing was saturated with urine. A cystoscopic examination revealed a circular opening, about two centimeters in length, in the wall of the bladder, posterior to the right ureteral orifice. Within six hours after the cystoscopic examination, the patient had urinated. Within a few weeks the sinuses in the hip closed, and the patient made a good recovery. Castallo

SPONTANEOUS RUPTURE OF BLADDER

and Fetter⁹ have recently reported a case in which an extension of a tubo-ovarian abscess penetrated the bladder wall. Falk and Hochman¹⁰ (1939) collected 54 similar cases from the literature and reported three personal cases. In many of the cases the inflammatory mass was of gonorrheal origin.

A pathologically weakened bladder wall is predisposed to rupture. Cases are on record in which the immediate cause of the rupture was a sudden increase in the intra-abdominal pressure. Probably a normal, unobstructed bladder does not rupture from muscular contraction, except during pregnancy. The violent contractions of the abdominal muscles in the labor of childbirth has been the responsible factor in a few reported cases.

Torpin,¹¹ in 1940, reviewed the published cases of spontaneous rupture of the urinary bladder in pregnancy and labor and reported a personal case. He found some eight cases associated with retroverted incarcerated pregnant uterus at three or four months. He classified the cases of spontaneous rupture in parturition as those in which (1) rupture occurred immediately; (2) rupture was delayed; (3) rupture into the vagina resulted in a vesicovaginal fistula; and (4) bladder rupture complicated uterine rupture. He cited two cases in which the bladder ruptured spontaneously during labor and four cases in which the bladder ruptured on the fourth to the tenth postpartum day. An additional case of the latter kind has since been reported by Claye¹² (1941). Torpin found one case in which the bladder ruptured into the vagina, resulting in a vesicovaginal fistula, and he reported a similar case of his own. His patient had had a vesicovaginal fistula since the birth of her fourth child, two months previous to the time he had examined her. During those two months her urine flowed from the vaginal orifice. At operation extensive lacerations were found, the anterior vaginal wall and the posterior bladder wall having been laid open in the midline from above the trigone down to the urethral sphincter. Reparative procedures were carried out, and the patient made a good recovery. Torpin based his discussion of the reported cases of urinary bladder rupture complicating uterine rupture on a series of 52 cases collected from the literature by Hagenbuck,¹³ in 1925. He considered that many of Hagenbuck's cases were traumatic but that possibly 17 were spontaneous ruptures.

Spontaneous rupture of the bladder is divided into two classes, according to whether the rupture is intra- or extraperitoneal. The former is much more frequent and at the same time is far more grave. Among the 20 cases of spontaneous rupture which Sisk and Wear⁴ found reported in the literature between the years 1900 and 1929, only four were extraperitoneal. Morbid changes in the bladder wall are a frequent finding in the extraperitoneal type, and an infrequent finding in the intraperitoneal type.

The symptoms and physical signs will vary depending upon whether the rupture is intra- or extraperitoneal. In the latter type the onset will be insidious, with few signs of shock. A bagginess will be noticed above the

pubis and in the groins, at times extending as high as the umbilicus. The patient will be able to void small amounts of urine, which will show some blood. In the intraperitoneal type of rupture the onset will be more sudden, and there will usually be early signs of shock. The later symptoms will be mainly those of peritoneal irritation; that is, severe abdominal pain, nausea and vomiting, and abdominal distention, rigidity and tenderness. A history of marked distention with a sudden collapse of the bladder can often be elicited. The patient will have an urgent desire to urinate, but will usually be unable to void more than a few drops. The evacuation of a very small or very large quantity of bloody urine by catheter is a significant early finding.

In the diagnosis of both types of rupture, the presence of urinary obstruction is an important indication of rupture. A cystoscopic examination is not practical, as a ruptured bladder can rarely be visualized. A cystogram taken after the injection of either iodized oil or air will sometimes reveal the point of leakage. The diagnostic test of introducing a measured amount of fluid into the bladder and comparing this amount with the quantity recovered is not infallible. When the rupture in the bladder is large, a great deal more fluid may be recovered than has been put in. If the disproportion either way is great and the urine is bloody, a rupture may be suspected.

The treatment of both intra- and extraperitoneal rupture is immediate operation. Early operation gives a very low mortality rate. Adequate urinary drainage is a most important measure in both types of rupture. In the treatment of the extraperitoneal rupture, drainage should be provided by means of a suprapubic tube. Closure of the bladder rent is not necessary, but it is certainly a desirable procedure if the condition of the patient permits its being carried out. Healing will be rapid, provided the drainage is adequate. In the treatment of the intraperitoneal rupture, the abdomen should be opened, the fluid contents aspirated, and the peritoneal cavity closed without drainage. The perforation in the bladder should be closed in layers. Urinary drainage should be provided by an indwelling urethral catheter or by a suprapubic tube, preferably the former.

The prognosis is good in the extraperitoneal type of rupture. According to Dittrich,¹⁴ among the untreated cases of extraperitoneal rupture, only 27 per cent are fatal. The outlook in the intraperitoneal cases becomes grave after the first 24 hours. The cause of death is either peritonitis or uremia, or both.

SUMMARY

1. The term, spontaneous rupture of the urinary bladder, is now the accepted designation for all nontraumatic ruptures of the bladder.
2. Spontaneous rupture is relatively rare, comprising about four per cent of the reported cases of bladder rupture.
3. A case is reported of a second spontaneous rupture of the posterior fundus of the urinary bladder. This case seems to be the only one of its

kind to be reported. The patient was an alcoholic, with a history of having been treated for syphilis. The etiology is obscure. At operation, the rent in the bladder wall was sutured and adequate drainage of the bladder was provided. The patient recovered.

4. The most frequent etiologic factors in bladder rupture are: (1) Hyperdistention from obstruction; (2) degenerative changes in the bladder wall from chronic distention; (3) pathologic changes in the musculature due to diseases of the bladder or to the extension of neoplastic or inflammatory diseases in adjacent structures.

5. The symptoms and physical signs vary, depending upon whether the rupture is intra- or extraperitoneal.

6. In the treatment of both types of rupture, early operation and the establishment of adequate urinary drainage are imperative.

7. The prognosis in intraperitoneal rupture becomes grave if operation is delayed longer than 24 hours.

REFERENCES

- ¹ Rivington, Walter: Rupture of the Urinary Bladder. (Hunterian Lecture). Med. Press and Circular, II, 434-436, November 22, 1882.
- ² Houel, Charles Nicholas: Des plaies et des ruptures de la vessie. Paris, Germer-Bailliere, 1857.
- ³ Goldenberg, Theodor: Beitrag zur Pathologie der Harnblasen-rupturen. Beitr. z. klin. Chir., 61, 350-371, January, 1909.
- ⁴ Sisk, Ira R., and Wear, John B.: Spontaneous Rupture of the Urinary Bladder. J. Urol., 21, 517-521, April, 1929.
- ⁵ Besley, Frederic A.: Rupture of the Urinary Bladder: Report and Analysis of Twenty-three Cases from the Records of Cook County Hospital. Surg., Gynec. and Obst., 4, 514-532, April, 1907.
- ⁶ Baumer, K.: On Spontaneous Rupture of the Bladder. Thesis, University Leipzig, 1913.
- ⁷ Stone, Eric: Spontaneous Rupture of the Urinary Bladder: Report of Two Cases. Arch. Surg., 23, 129-144, July, 1931.
- ⁸ Wilson, Leonard L.: Spontaneous Rupture of the Urinary Bladder in a Tabetic Patient. Med. Bull. Vet. Admin., 17, 93-95, July, 1940.
- ⁹ Castallo, Mario, and Fetter, Theodore R.: Perforation of Tubo-ovarian Abscess into the Urinary Bladder: Report of a Case. Urol. and Cutaneous Rev., 55, 425-427, July, 1941.
- ¹⁰ Falk, Henry C., and Hochman, Samuel: Rupture of Pelvic Inflammatory Masses into the Urinary Bladder. Am. J. Obst. and Gynec., 38, 654, October, 1939.
- ¹¹ Torpin, Richard: Spontaneous Rupture of the Urinary Bladder in Labor: Case Report, Literature, and New Classification. Urol. and Cutaneous Rev., 44, 553-557, September, 1940.
- ¹² Claye, A. M.: A Case of Puerperal Retention of Urine Causing Traumatic Rupture of the Bladder and Death. J. Obst. and Gynec. Brit. Empire, 43, 235-238, April, 1941.
- ¹³ Hagenbuck, M.: Über Uterusrupturen mit Blasenriss im Anschluss an eigenen Fall. Ztschr. f. Geburtsh. u. Gynak., 39, 211-228, 1925.
- ¹⁴ Dittrich, Rudolf: Über spontane Harnblasen-rupturen. Deutsche med. Wchnschr., Leipz. u. Berl., 48, 974-975, July 21, 1922.

PREOPERATIVE SCRUBBING IN ABDOMINAL SURGERY

II—CLINICAL STUDIES

J. K. BERMAN, M.D.

INDIANAPOLIS, INDIANA

FROM THE DEPARTMENT OF SURGERY, INDIANA UNIVERSITY SCHOOL OF MEDICINE, AND THE SURGICAL SERVICES OF THE UNIVERSITY HOSPITALS, INDIANAPOLIS, IND.

IN A PREVIOUS COMMUNICATION¹¹ we reported the effects of preoperative scrubbing as a protective measure in the prevention of wound infection when tried in experimental animals. It was found to have some value when done 96 to 120 hours before surgery. It was, perhaps, deleterious when done 12 to 24 hours before operation. This study is herewith continued in patients.

In the Indiana University Hospitals most patients are prepared for abdominal surgery as follows: On the night before operation the abdomen is shaved, scrubbed with soap and water on gauze and painted with tincture of merthiolate. Sterile towels are placed over the field and secured with adhesive tape. The incidence of postoperative wound infection has been extremely low with this routine.

By preoperative scrubbing we mean any preparation up to 12 hours before operation. Immediate surgical sterilization is not included in this study. Preoperative "scrubbing" in the University Hospitals is not done in the surgical sense. It is carried out in the manner described, without regard to the length of time or the use of a brush, and must be regarded as a cleansing process only.

The effect of scrubbing, as defined, is difficult to prove clinically. Therefore, patients with intestinal fistulae were selected because there could be no doubt of contamination at the time of surgery or shortly thereafter. Five patients with intestinal fistulae from various causes were selected for this study.

CASE REPORTS

Case 1.—A female, age 37, was admitted to the Long Hospital complaining of a fecal fistula in an old operative scar. She had been operated upon elsewhere for "pelvic infections." The abdominal wall was excoriated and bathed with intestinal content. The diagnosis was postoperative intestinal fistula of the small bowel. The patient was placed on a Bradford frame in the prone position for two weeks. This permitted the excoriated skin to heal.

Four days before operation the abdominal wall was scrubbed with soap and water for ten minutes. Immediately before operation the abdomen was again scrubbed with tincture of green soap and sterile water and washed with 70 per cent alcohol (by weight), as described by Price.^{1, 2} The operation was extensive, requiring multiple resections of the small bowel, with anastomoses. The abdominal wound was closed as follows: No. 00 chromic catgut in the peritoneum (interrupted mattress), No. 000 in the muscle (interrupted), No. 00 chromic catgut in the fascia (figure-of-eight

SURGICAL SCRUBBING

stitch), and interrupted silk stitches in the skin, leaving about a one-quarter-inch gap between the edges. All the suture lines healed *per primam* except the skin which healed by second intention although there was a minimal amount of infection.

Case 2.—Mrs. N. F., a white female, age 36, had suffered from chronic ulcerative colitis for about eight years. Medical treatment had failed to control the course of the disease. An ileostomy was performed in November, 1941. Three weeks later the ascending, transverse and descending colon down to the sigmoid was removed. A wound infection due to colon bacilli developed four days postoperative, and an abscess formed, which was drained. However, she continued to pass blood and mucus per rectum. She was admitted to the Long Hospital for a third-stage operation in April, 1942.

Five days before surgery the abdomen was scrubbed with soap and water for eight minutes. The operation was performed April 28, 1942. Immediate preparation

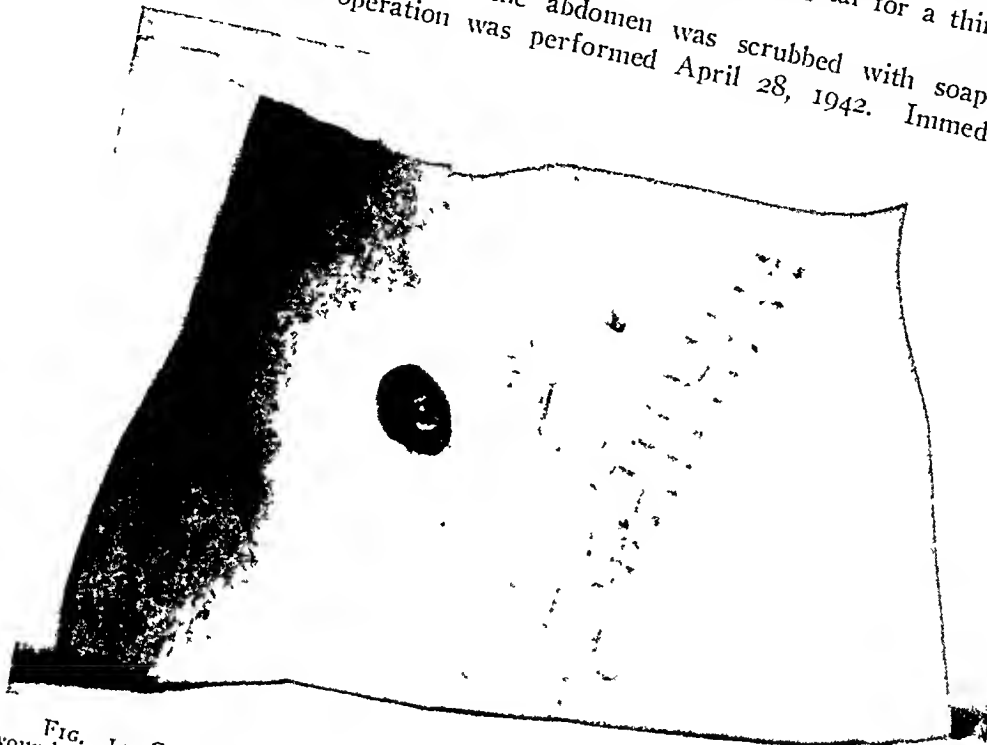


FIG. 1.—Case 2: Abdomino perineal resection showing ileostomy and surgical wound on the 8th postoperative day. The incision has healed *per primam*.

of the abdomen was exactly as in the previous case. An abdomino-perineal resection was performed, removing all of the remaining colon, rectum and anus. The wound was closed as in Case 1 except that the skin and subcutaneous tissue were closed snugly. The wound was protected with adhesive which was covered with zinc oxide ointment. However, some fecal drainage seeped under the dressing. On the eighth postoperative day stitches were removed. The wound had healed *per primam* (Fig. 1).

Case 3.—Mrs. A. H., a white female, age 41, had a pelvic operation elsewhere in 1938 for what she described as "pus tubes." One week postoperative she developed a persistent diarrhea and fecal drainage from her abdominal incision. This continued to drain and, three months later, a second operation was performed in an effort to close the fecal fistula. At this time she was having chills and fever. Smears and sections were taken from the fistula but no tuberculous or fungus infection was found. Although closure was effected, the fistula recurred and, April 30, 1940, a third operation was performed in an effort to close the fistula. On November 15, 1940, the wound again began to drain fecal material and, in addition, the same material was found to be draining from the vagina. She was admitted to the Long Hospital for diagnosis and treatment. Careful study and roentgenologic examination with iodized oil

injection revealed multiple communicating fistulae. On June 30, 1941, a left inguinal colostomy was established. The patient did not return for treatment until July 15, 1942. At this time a lipiodol injection and roentgenologic study showed a fistulous tract which communicated with the sigmoid, the bladder, the vagina and the anterior abdominal wall.

Four days prior to surgery the abdominal wall was scrubbed with soap and water for eight minutes. On the night before operation the abdomen was again scrubbed with soap and water for three minutes. Immediate preparation before surgery was exactly as in the first patient. The fistulous tracts were completely excised, and the abdominal wall was closed without drainage. One Penrose drain was brought through the posterior cul-de-sac into the vagina. The operation was successful, and the abdominal wound healed *per primam*, without infection.

Case 4.—K. W., a white female, age 54, was admitted to the Long Hospital, July 1, 1942, with a diagnosis of intestinal obstruction. She had had a pelvic operation 12 years previously. The diagnosis of intestinal obstruction was confirmed and she was operated upon. At operation, a band of adhesions was encountered extending from a loop of small bowel to the right broad ligament. Beneath this band 97 cm. of small intestine had become strangulated and was gangrenous. It was resected and both ends of the bowel were anchored to the peritoneum and secured in the manner of a double-barrel enterostomy. The abdominal wall became excoriated after two weeks. The patient was placed upon a Bradford frame in the prone position. All excretions were collected in a bed pan placed beneath the enterostomy stoma. The excoriation became greatly reduced.

Four days before the second operation for the closure of the enterostomy, the patient was scrubbed for eight minutes, in the manner previous described. On July 27, 1942, the wound was reopened and the ends of the bowel freed, inverted, and brought together by a lateral anastomoses. The peritoneum was closed with chromic No. 00 catgut and everted with interrupted mattress sutures. The muscle was brought together with interrupted sutures of the same material. The fascia was closed, with the same material, by an interrupted cross-stitch, with buried knots. The subcutaneous tissue was loosely approximated with No. 000 chromic catgut and a one-quarter-inch gap was allowed between the edges of this tissue. The skin was held with interrupted silk and it, too, was allowed to gape one-quarter inch. The skin edges remained apart although there was a minimal amount of infection.

Secondary closure was undertaken under one per cent novocain anesthesia. The skin was cleansed with soap and water and washed with sterile normal saline solution, then brought together with interrupted silk sutures. The wound healed *per primam*.

Case 5.—J. L., a female, age 26, was admitted to the Long Hospital in July, 1942, with the history that in September, 1940 a pelvic operation was performed elsewhere; 15 days after the operation the incision opened and drained fecal matter; and this had persisted up to the time of admission. The diagnosis was postoperative fistula of the small bowel.

The abdomen was scrubbed four days before the operation, as had been done in the previous four cases. Immediate preparation was exactly as in Case 1. At operation, the fistula was excised and found to communicate with a loop of ileum. The opening into the bowel was trimmed away and turned in with silk sutures. The abdominal incision was washed with normal salt solution and was closed without drainage. The wound healed *per primam*.

This study leads us to believe that stitch, subcutaneous and skin infections, generally, are less common in the repair of abdominal fistulae with preliminary scrubbing of the abdominal wall four days before operation, if attention is given to other factors in the healing of contaminated wounds. These factors are (1) the avoidance of excessive trauma; (2) washing of the wound with

SURGICAL SCRUBBING

1000 cc. of sterile normal saline before closure; and (3) incomplete closure of the skin and subcutaneous tissue. Perhaps it is the local immunity that develops due to the constant presence of bacteria which aids in the healing *per primam* in most of these cases. However, this was not as apparent prior to our scrubbing technic. There have been no patients with dehiscence of the wound since the adoption of this procedure.

DISCUSSION.—Scrubbing with a brush, soap and water removes the transient bacterial flora from the skin readily but the resident flora more slowly. Price has shown that in eight minutes of scrubbing the bacterial flora on the hands and arms is reduced about 50 per cent. Although soap and water is not strongly bactericidal its usefulness in the treatment of wounds has been proved beyond peradventure, and is due to its efficiency in removing foreign material and bacteria by the scrubbing.^{5, 6, 7} However, this is not a factor in our cases. The abdomen was covered with sterile towels after preparation but not in a manner which would exclude bacteria. If there is any effect whatever from the procedure, it is the protective reaction. In tissue induced by the scrubbing which invites the prophylactic use of vaccines in this regard, it is possibly comparable to the prophylactic use of vaccines in the peritoneal and joint cavities (bacterial trauma), beef broth in the pleural cavity, tincture of iodine on the skin, or sulfonamide drugs in surgical wounds as a prophylactic measure (chemical trauma). It will be noted from our discussion that experimental and clinical results have not been very conclusive. However, from these observations we may deduce that preliminary scrubbing 24 hours before operation, even with protective coverage of sterile towels, is not effective in the prevention of infection from gross contamination or injury to tissue. Furthermore, it has been shown that bacteria are present in the abdominal wall after scrupulous preparation.⁸ These residual bacteria will continue to grow after scrubbing and will be present on the next morning in numbers equal to those which have been removed the night before.

One of the most common causes for delayed wound healing is infection. It is, also, a threat to the life of the patient who has been operated upon. Perhaps we have been concentrating too much on the activities of the invading organism and its exclusion or annihilation rather than the resistance of body tissue to these organisms.⁹ Even in clean wounds made under so-called aseptic conditions, bacteria are present.⁷ Since their complete exclusion is impossible under the most favorable conditions, it behooves us to study nature's power to combat the invasion of micro-organisms. The mere presence of bacteria (contamination) does not constitute an infection. Only if they invade, multiply, and destroy cells, are they of importance. Two factors must be considered: First, the invading organism; and, second, the ability of the tissue to prevent their growth. In the latter may be included trauma to tissue which lowers resistance along with such factors as provide a high degree of immunity in certain areas. This study does not question

the necessity for immediate preoperative preparation of the abdominal wall, nor the type of preparation which may be employed, nor does it imply that any of the aseptic precautions of modern surgery be relaxed. Our study shows that scrubbing the abdomen for eight minutes 24 hours before surgery with soap and water in the experimental animal or in the human patient, apparently does not increase the local resistance of tissue, or eliminate the invading organism sufficiently to prevent infection in surgical wounds in the presence of gross contamination. If carried out 96 to 120 hours before surgery it is, perhaps, useful in increasing local tissue resistance, although there is no direct proof of this. In the presence of gross contamination it is better to close the skin and subcutaneous tissue with a wide gap, as we have always done, or to leave it open entirely, as recently advocated by Collier and Volk.¹⁰

In all grossly contaminated surgical wounds there must be provision for drainage. This should be made without resort to drains which act as a foreign body and predispose to infection.

A clinical study of so few cases is not conclusive. However, this is a preliminary report, written with the hope that others may help the author to properly evaluate the procedure.

CONCLUSIONS

1. The use of preoperative surgical scrubbing of the abdomen in patients with fecal fistula does not interfere with wound healing when employed 96 to 120 hours before surgery.

2. It probably affords some increase in local immunity due to the stimulation of the blood supply. But it must never be relied upon to prevent infection in the presence of gross contamination. In such cases there must be provision for skin and subcutaneous drainage by very loose closure and no drainage tubes.

3. Scrubbing 12-24 hours before surgery has no demonstrable effect on local immunity.

REFERENCES

- ¹ Berman, J. K., Sage, Charles, and Ballenger, Felix: Chronic Idiopathic Ulcerative Colitis Treated by Total Colectomy. *Quart. Bul. Ind. Univ. Med. Center*, 4, 77-81, July, 1942.
- ² Price, P. B.: Bacteriology of Normal Skin: A New Quantitative Test Applied to a Study of the Bacterial Flora and the Disinfectant Action of Mechanical Cleansing. *J. of Infec. Dis.*, 63, 301-318, 1938.
- ³ Price, P. B.: Ethyl Alcohol as a Germicide. *Arch. of Surg.*, 38, 528, March, 1939.
- ⁴ Lane, C. Guy, and Blank, Irvin H.: Cutaneous Detergents. *J. A. M. A.*, 118, 804, March 7, 1942.
- ⁵ Koch, S. L., and Mason, M. L.: Division of the Nerves and Tendons of the Hand. *S. G. & O.*, 56, 1-39, 1933.
- ⁶ Reid, M. R., and Carter, B. N.: The Treatment of Fresh Traumatic Wounds. *ANNALS OF SURGERY*, 114, 4-18, 1941.

SURGICAL SCRUBBING

- ⁷Berman, J. K.: Synopsis of Principles of Surgery. C. V. Mosby Co., p. 24, 47 and 278, *etc.*
- ⁸Ives, H. R., and Hirschfeld, J. W.: Bacterial Flora of Clean Surgical Wounds. *ANNALS OF SURGERY*, 107, 607, 1938.
- ⁹Berman, J. K.: Critical Evaluation and Present Status of the Theory of Focal Infection. *J. Ind. State Med. Assoc.*, 21, 665, December, 1931.
- ¹⁰Coller, F. A., and Volk, W. L.: The Delayed Closure of Contaminated Wounds: A Preliminary Report. *ANNALS OF SURGERY*, 112, 256-270, August, 1940.
- ¹¹Berman, J. K., Houser, Alan D., and Kurtz, Wm. A.: Preoperative Scrubbing in Abdominal Surgery: I—Experimental Studies. *ANNALS OF SURGERY*, 117, 535-543. April, 1943.

CLINICAL USES OF VITALLIUM

CHARLES S. VENABLE, M.D., AND WALTER G. STUCK, M.D.

SAN ANTONIO, TEXAS

SINCE PIONEER SURGEONS began to contrive operations of various types, there has been a keen interest in the use of metallic appliances to aid in supporting tissues. Metal cleft palate plates, bone plates, screws, wire, skull replacements, intestinal anastomosis tubes, cannulae, and many other metallic contrivances have been devised to aid the surgeons in reconstructing some defect in the body. Scores of implements made of nearly every known

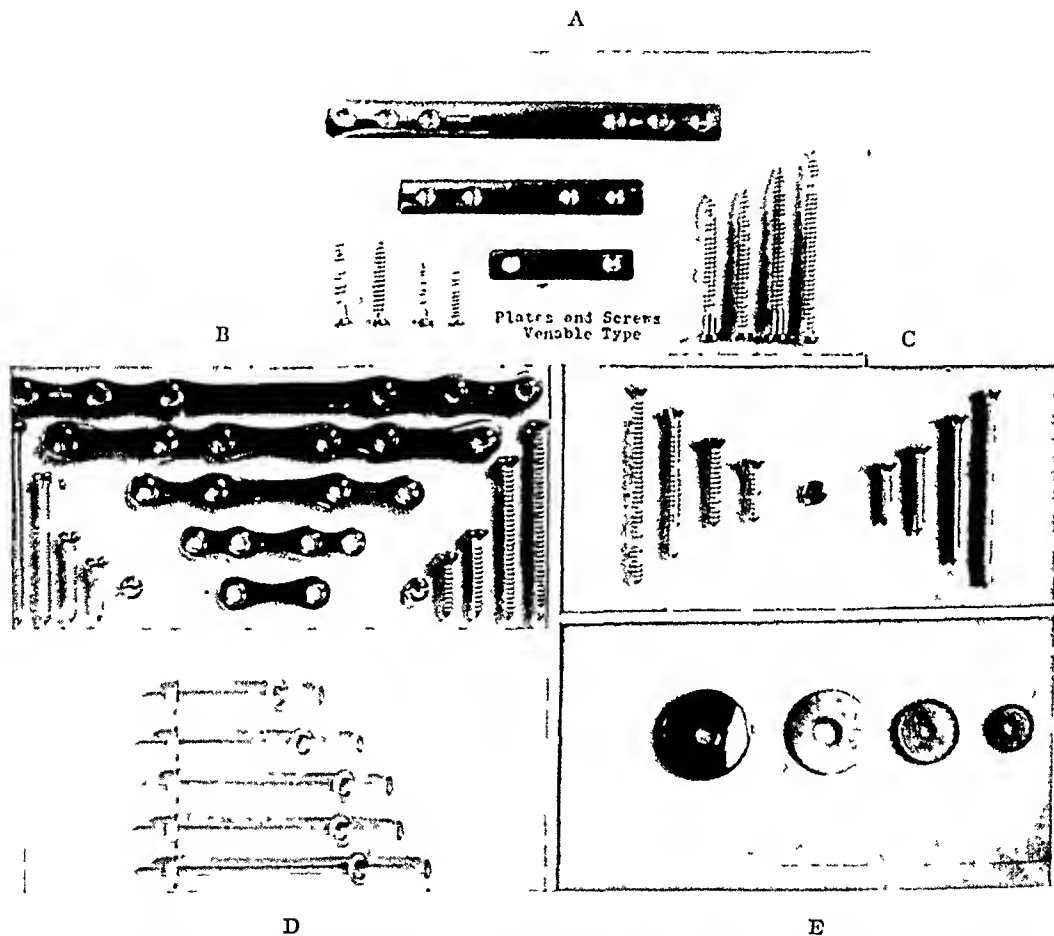


FIG. 1.—(A) Curved metal plates and flat-headed screws of Vitallium designed by Venable for use in bone surgery. (B) Sherman-type plates and machine screws made of Vitallium. (C) Vitallium screws of the wide thread type, made with Phillips recessed heads, which provide a much firmer grip for the screwdriver. (D) Vitallium bolts devised by Barr for fractures of the tibial plateau. (E) Vitallium washers, prepared to supplement bolts and screws in the fixation of fractures.

metal have been conceived and utilized at one time or another. Nevertheless, in spite of this long search for suitable metal devices for use in surgery, there was slight success and metals came to be discarded because they seemed to be "foreign bodies" that were poorly tolerated by the tissues.

With the introduction of the alloy, Vitallium, into bone surgery in 1936,

CLINICAL USES OF VITALLIUM

we were able to present a metal which was inert in the body fluids and consequently free of any unfavorable tissue reactions. Moreover, we were able to establish the principle that no metal is suitable in the body if it is subject to corrosive change due to chemical or electrolytic action in the tissue

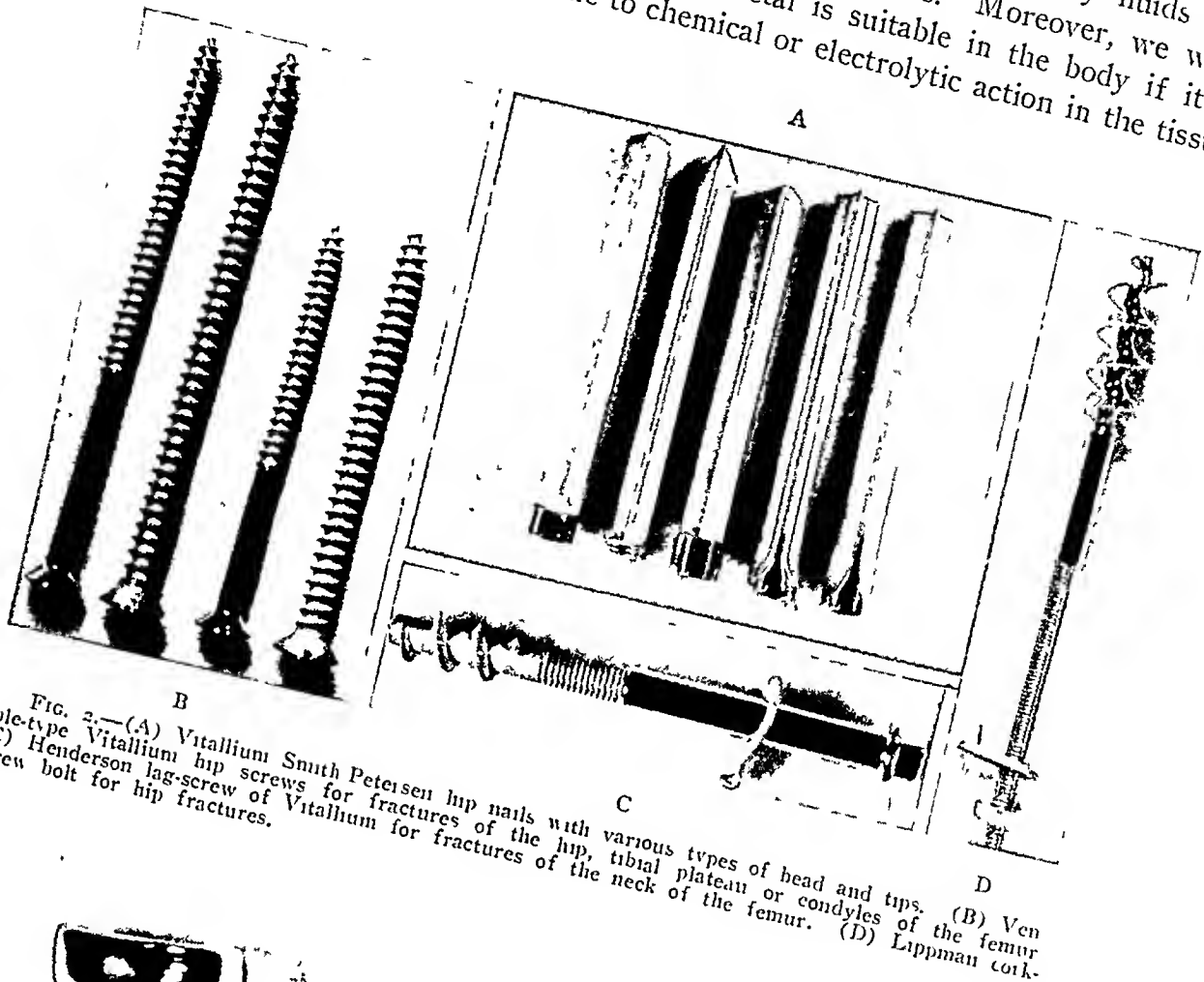


FIG. 2.—(A) Vitallium Smith Petersen hip nails with various types of head and tips. (B) Venable-type Vitallium hip screws for fractures of the hip, tibial plateau or condyles of the femur. (C) Henderson lag-screw of Vitallium for fractures of the neck of the femur. (D) Lippman cork-screw bolt for hip fractures.



CAPS FOR HEAD OF RADIUS



FIG. 3—Kellogg Speed's Vitallium cap for the head of the radius.

fluids. The recognition of the results of electrolytic action between metals in the body as a cause of failure of metal appliances was a concept which had been suggested previously by others, but discarded by them since it was not clearly understood that corrosion is dependent upon electrolytic action. That electrolytic action accompanied unfavorable tissue reaction, we found to be uniformly true and the elimination of electrolytic action through use of

a metal which resisted chemical effects of body fluids eliminated the usual damage. Our first animal experiments on electrolysis of metals in the body were undertaken in 1935-36, wherein we came upon Vitallium, a dental alloy, which had been developed by the Austenal Laboratories because of its entire corrosive resistance to saliva. After demonstrating that Vitallium was inert or passive in the body fluids of animals, we had plates and screws made to use in human bones. The first clinical case was operated upon in

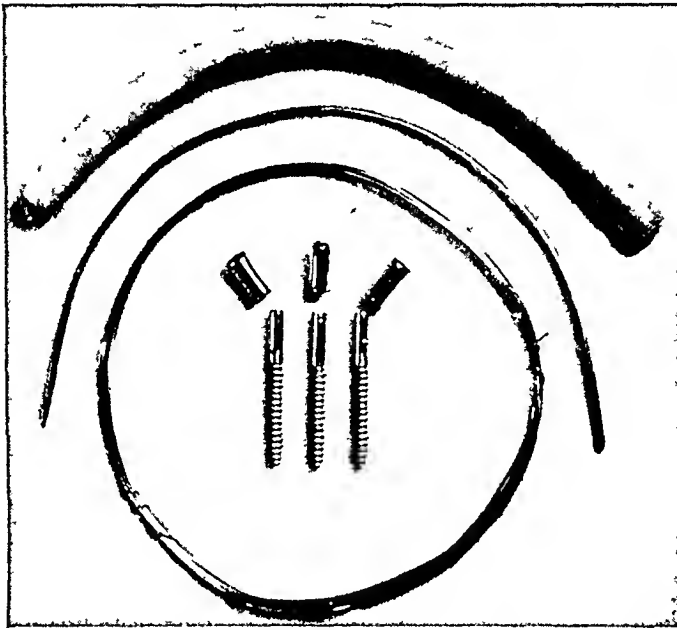


FIG 4—Berry's Vitallium screws for fractures of the mandible.



FIG 5—Bosworth's Vitallium coraco-clavicular screw

September, 1936, and since that time hundreds of operations have been performed by many surgeons in which Vitallium appliances have been used. After six years' experience in hundreds of cases, it is now well established that Vitallium is the most inert alloy currently used in surgery. As this record has become known, Vitallium appliances of diverse types have been designed by surgeons in other fields than orthopedic surgery. It is this development which we wish to report to demonstrate the protean utility of

CLINICAL USES OF VITALLIUM

this alloy and its complete tolerance to the various fluids and secretions of the body because of its chemical and electrolytic inertness.

FRACTURES

In traumatic surgery, bolts, screws, and plates of Vitallium have been found to be most useful in repairing fractures which could not be maintained in position by wires, kangaroo tendon, beef bone screws, or other less stable

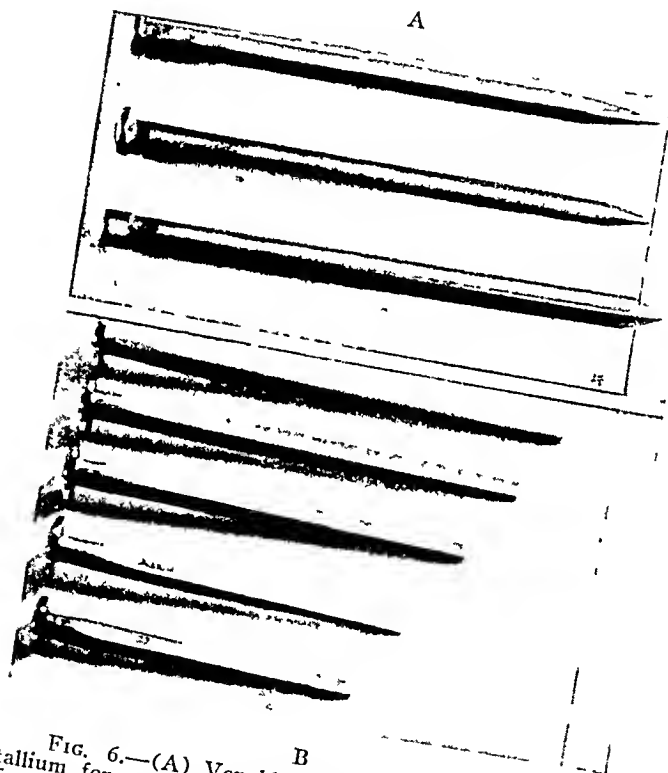


FIG. 6.—(A) Venable-Stuck square nails of Vitallium for arthrodesing joints and to secure condylar fragments in fractures. (B) Vitallium Smith-Petersen arthrodesis pins to stabilize joints after fusion operations.

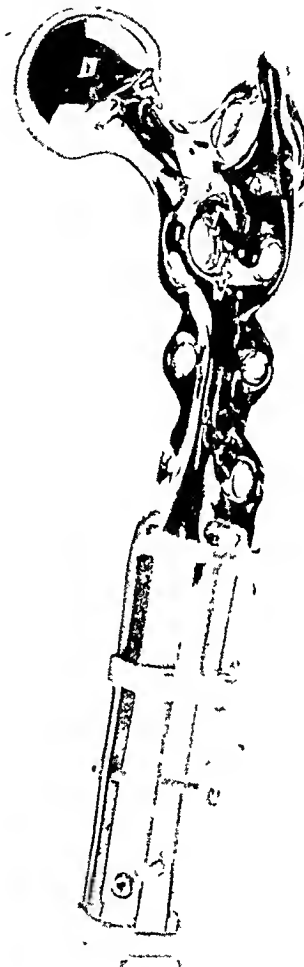
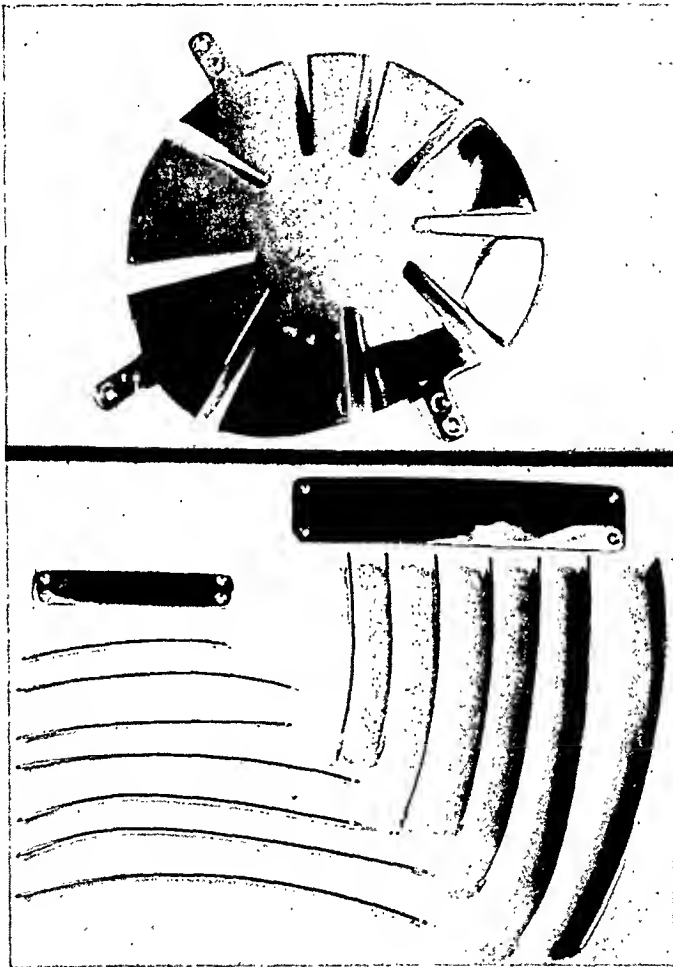


FIG. 7.—Vitallium replacement of the upper end of the femur, devised by Bohlman and Moore and used after resection for a malignant tumor.

materials. Fractures of long bones, intercondylar fractures into joints, and certain grossly displaced fractures, when replaced and anchored by Vitallium screws and plates have been found to heal more rapidly and with less disability than if treated by appliances of other metals (Fig. 1). The special problem of fracture of the hip has been nearly solved in recent years by the use of nails, screws, or pins to fasten the head fragment to the neck. This has lead to a much greater prospect of union of the fractures, has eliminated the need for hip spica encasements, has prevented

stiffness of the knee, and has generally given the victims much more comfort and hope of ultimate recovery. These large hip nails and screws often came loose or had to be removed because of unfavorable reactions about them. However, since they have been made of Vitallium, irritation of tissue has been eliminated and the need for the second operation of removal markedly diminished (Fig. 2).

A



B

FIG. 8.—(A) Geib-type Vitallium skull plate for the repair of cranial defects. (B) Vitallium strips devised by Claude Beck to cover defects in the skull.

After removal of the head of the radius for comminuted fracture or in arthroplasties of the elbow, a Vitallium radial cap, designed by Kellogg Speed, has been found to facilitate motion and prevent excess new bone formation (Fig. 3).

In fractures of the jaw, Berry has devised Vitallium screws which are anchored in the fragments to support them in the correct position during healing and to prevent displacement (Fig. 4).

CLINICAL USES OF VITALLIUM

For acromioclavicular separations where the ligaments are severely lacerated, Bosworth's screw of Vitallium has been found to be useful in fastening the end of the clavicle to the scapula (Fig. 5).

For the reattachment of small fracture fragments or to anchor joints after arthrodesing operations, several types of round, square, and flanged nails of Vitallium have been devised to aid in the operation (Fig. 6).

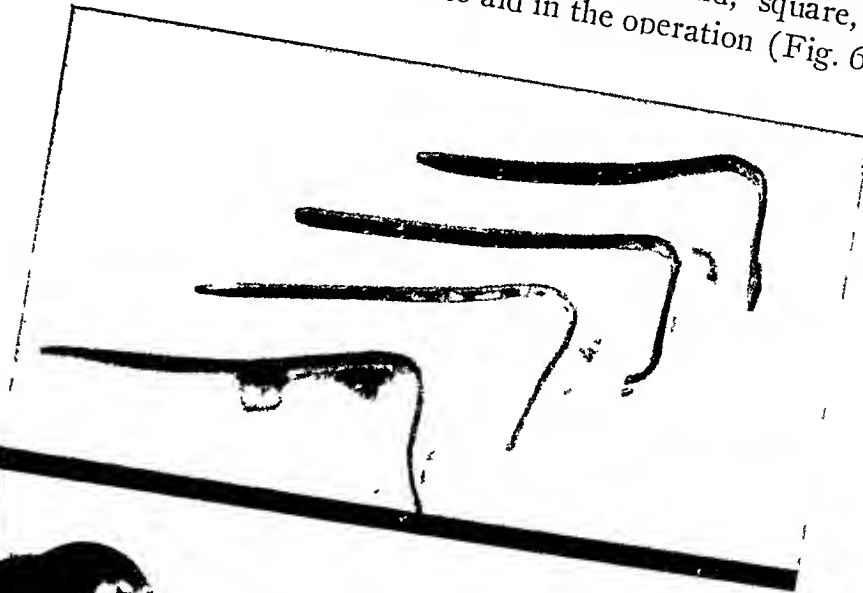


FIG 9



FIG 10

FIG 11

FIG. 9.—Kimball's Vitallium nasal skeletal supports for the repair of "saddle nose" deformity.
FIG. 10.—Doherty's Vitallium orbital implants.
FIG. 11.—Bowers' Vitallium testicle replacement.

TISSUE REPLACEMENT

The most spectacular use of a Vitallium appliance to replace lost tissue was Bohlman and Moore's metal head and neck of the femur. After the entire upper end of the femur had been resected for a malignant tumor, a Vitallium replacement was inserted which functioned normally. The patient was thereby given a strong, stable, painless hip on which he walked for several years (Fig. 7).

For defects of the skull, Vitallium plates serve as dependable, comfortable protectors of the adjacent soft tissues without the usual headaches (to surgeon

and patient) and irritation that follow most other replacements. Geib devised a plate which was modeled to fit the defect under consideration, while Claude Beck developed various sizes of Vitallium strips which could be used without preliminary preparation (Fig. 8).

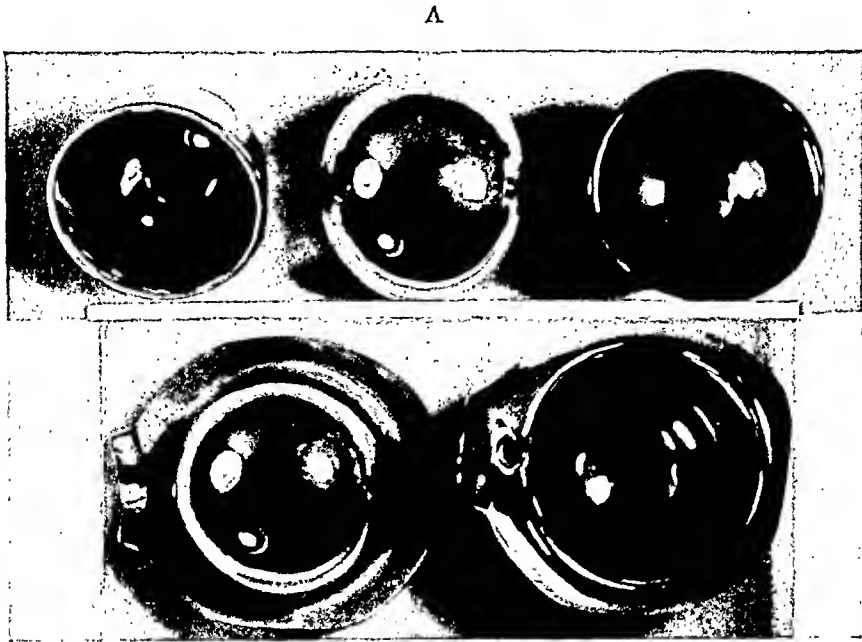


FIG. 12.—(A) Smith-Petersen Vitallium hip caps for repair of ankylosed joints or those in which there has been much destruction of the joint surface. (B) Albec-Preston Vitallium hip sockets for arthroplasty of the hip.

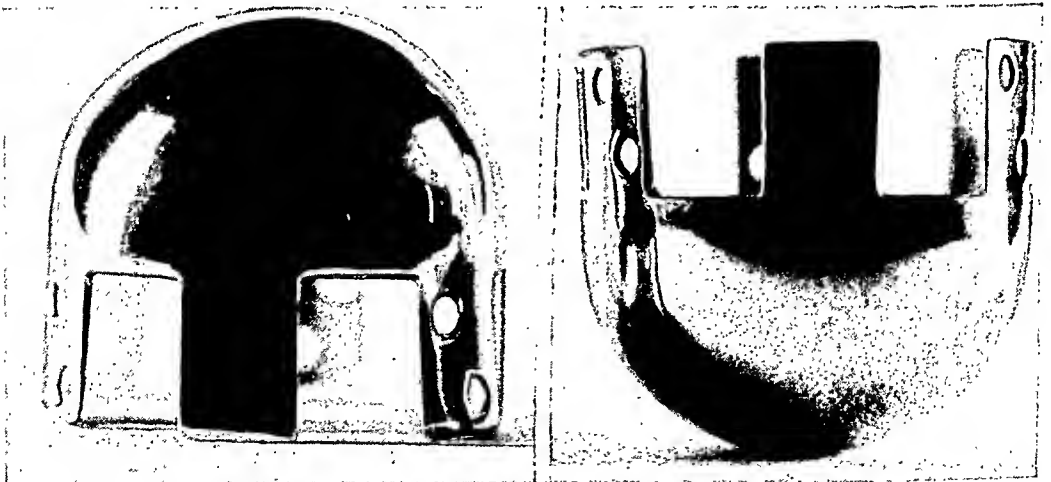


FIG. 12(C).—Venable-type hip cap which is secured by flanges and screws to the neck of the femur.

The bridge of the nose often loses its bony support after osteomyelitis or congenital lues, which results in the classical "saddle nose" deformity. During plastic operations to repair the defect, a Vitallium support has been

CLINICAL USES OF VITALLIUM

used to restore the normal contour while holding the external skin in position (Fig. 9).
After enucleation of the eye, some implant is needed to preserve the skin folds and provide a foundation for an artificial eye. Many materials have been utilized, though Doherty feels that the Vitallium replacement is more comfortable and secure than any of the previous appliances (Fig. 10).

FIG. 13.

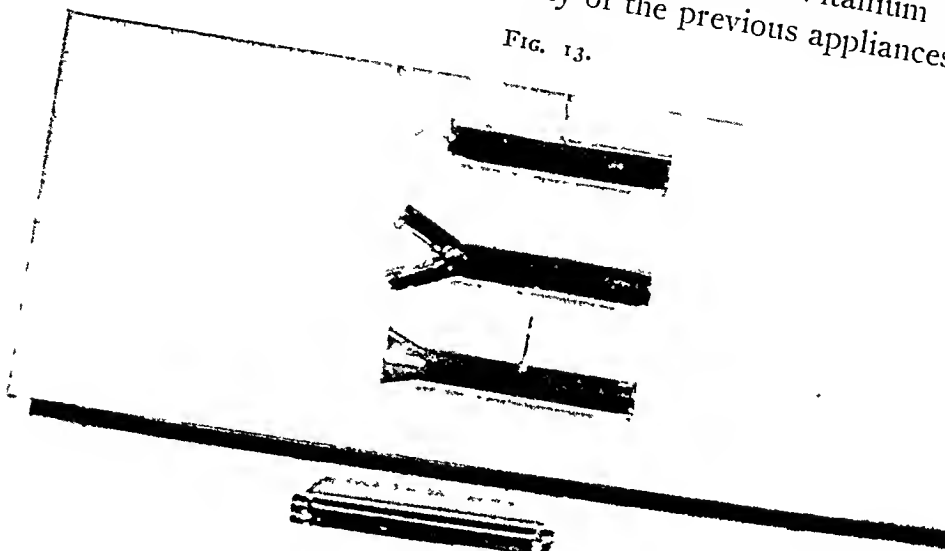


FIG. 14.

FIG. 13.—Pearse Vitallium tubes for repair of the bile ducts.
FIG. 14.—Lord's Vitallium tubes for repair of strictures of the ureter.



FIG. 15.—Smith's colostomy plug of Vitallium to be worn externally over a colostomy stoma.

When the testicle is removed for any reason, it is desirable to replace the defect to overcome unsatisfactory psychologic reactions. Vitallium implants have been found most satisfactory since they are light in weight and nonirritating, though patients notice that they are cold (Fig. 11).

ARTHROPLASTY OF JOINTS

The problem of restoring motion to ankylosed joints has occupied the attention of surgeons for many years. Pieces of fascia lata, pig bladder, and fat, have been used with varying degrees of success as an interposing material. Since the introduction of Vitallium, metal appliances have been used to line the hip, knee, elbow, and finger joints. The most successful of these metal joints is the hip, because this joint is more simple mechanically and is better suited to such reconstructive procedures. Venable devised a fixed type of Vitallium hip cap, while Smith-Petersen has advocated the free floating type (Fig. 12).

BILE DUCT TUBES

Pearse and Clute have devised Vitallium tubes to place in the bile ducts for the repair of strictures or to replace irreparable damage to the ducts. This is the first material which has been found that will resist the action of bile and still cause no irritation to the adjacent soft tissues. The success of these bile tubes has opened new vistas in the surgical replacement or repair of damaged digestive or excretory organs (Fig 13).

URETER TUBES

The problem of repairing or replacing portions of a ureter requires that a tube will maintain its normal lumen without any incrustation and be free of any other irritative phenomena. Vitallium tubes have been used successfully for this purpose as well as for the maintenance of permanent suprapubic cystotomies (Fig. 14).

COLOSTOMY PLUG

While a colostomy plug is not an application of metal within the body, still, it necessitates a material which will resist the intestinal contents and at the same time rest against the abdominal wall without causing irritation of the skin. Smith's colostomy plug of Vitallium seems to meet all these requirements and to be far superior to any other materials which have been used heretofore (Fig. 15).

SUMMARY

It has been more than six years since we demonstrated the effects of electrolysis of metals in the body and introduced the inert alloy, Vitallium, into surgery. During this time, many uses have been found for Vitallium where a passive metal appliance was desired. While there are numerous devices which have been made of Vitallium that have not yet been reported by their sponsors, we are presenting some of those which are better known to show the wide range of usefulness of this metal. In many of these locations, no metal has previously been available which could be used with success because of harmful electrolytic effects.

CLINICAL USES OF VITALLIUM

BIBLIOGRAPHY

- ¹ Albee, F.: A New Vitallium Cup for Arthroplasty of the Hip. Jour. Internat. Coll. of Surg., 4, 289-293, 1941.
- ² Barr, J. S.: Treatment of Fractures of External Tibial Condyle. J. A. M. A., 115, 1683-1687, 1940.
- ³ Berry, H. C.: A New Departure from Orthodox Methods of Setting Fractured Edentulous Mandibles. Jour. Amer. Dental Assn., 28, 388-392, 1941.
- ⁴ Bigelow, H. M.: The Treatment of Fractures of the Mandible with Vitallium Screws. Med. Bull. Vet. Adm., 17, 54-56, 1940.
- ⁵ Bosworth, B. M.: Acromioclavicular Separations. Surg. Gynec. & Obst., 72, 667-669, 1941.
- ⁶ Burman, M. S.: Vitallium Cap Arthroplasty of Metacarpophalangeal and Interphalangeal Joints of the Fingers. Bull. Hosp. for Joint Dis., 1, 79-89, 1940.
- ⁷ Campbell, W. C., and Speed, J. S.: The Use of Vitallium as a Material for Internal Fixation of Fractures. ANNALS OF SURGERY, 110, 119, 1939.
- ⁸ Campbell, W. C.: Interposition of Vitallium Plates in Arthroplasties of the Knee. Amer. Jour. Surg., 47, 639-641, 1940.
- ⁹ Campbell, W. C., and Boyd, H. B.: Fixation of Onlay Bone Grafts by Means of Vitallium Screws in the Treatment of Ununited Fractures. Amer. Jour. Surg., 51, 748-756, 1941.
- ¹⁰ Clute, H. M.: Bile Duct Reconstruction With Vitallium Tubes. New England Jour. Med., 226, 484-487, 1942.
- ¹¹ Doherty, W. B.: A New Implantation Sphere Made of Vitallium. Arch. Ophthalm., 22, 337-338, 1939; *idem*: Orbital Implants: With Special Reference to Vitallium. Arch. Ophthalm., 25, 637-642, 1941.
- ¹² Geib, F. W.: Vitallium Skull Plates. J. A. M. A., 117, 8-12, 1941.
- ¹³ Girsdanský, J., and Newman, H. F.: The Use of A Vitallium Testicular Implant. Amer. Jour. of Surg., 53, 514, 1941.
- ¹⁴ Hopkins, H. H., and Zuck, F. N.: Arthroplasty of Hip With Use of Vitallium Cup. Med. Bull. Vet. Adm., 15, 1-2, 1938.
- ¹⁵ Jewett, E.: One-Piece Angle Nail for Trochanteric Fractures. Jour. Bone and Joint Surg., 23, 803-810, 1941.
- ¹⁶ Kimball, G. H., and Drummond, R. N.: Vitallium for Nasal Skeleton Support. Jour. Okla. Med. Assn., 34, 9-13, 1941.
- ¹⁷ Logsdon, C. M.: Utilization of Vitallium Appliances to Treat Edentulous Mandible Fractures. Jour. Amer. Dental Assn., 29, 970-978, 1942.
- ¹⁸ Lord, J. W., and Eckel, J. H.: The Use of Vitallium Ureter Tubes. Jour. Urol., (In press)
- ¹⁹ O'Donoghue, A.: The Phillips Recessed Head Screws. Amer. Jour. of Surg., 54, 758, 1941.
- ²⁰ Pearse, H. E.: Benign Stricture of the Bile Duct Treated with a Vitallium Tube. Surgery, 10, 37-44, 1941; *idem*: Vitallium Tubes in Biliary Surgery. ANNALS OF SURGERY, 115, 1031, 1042, 1942.
- ²¹ Secord, E. W., and Breck, L. W.: A Case in which a Vitallium Plate Could Not Be Removed. Jour. Bone and Joint Surg., 22, 749, 1940.
- ²² Smith, T. E.: Controlling Colostomies. Texas State Jour. of Med., 37, 241-245, 1941.
- ²³ Smith-Petersen, M. N.: Arthroplasty of The Hip: A New Method. Jour. Bone and Joint Surg., 21, 269-288, 1939.
- ²⁴ Speed, Kellogg: Hip Arthroplasty with Vitallium Cap. Western Jour. Surg. Gynec. & Obst., 48, 101-105, 1940; *idem*: Ferrule Caps for Head of Radius. Surg., Gynec. & Obst., 73, 845-850, 1941.
- ²⁵ Strock, A. E.: Experimental Work on a Method for the Replacement of Missing

- Teeth by Direct Implantation of a Metal Support Into the Alveolus. Amer. Jour. Orthodontics & Oral Surgery, 25, 467-472, 1939.
- ²⁶ Stuart, F. A.: The Use of Vitallium Screws in Fractures of the Long Bones. Jour. Okla. Med. Assn., 33, 8-11, 1940.
- ²⁷ Stuck, W. G.: Electrolytic Destruction of Bone Caused by Metal Fixation Devices. Jour. Bone and Joint Surg., 35, N. S. No. 19, 1077-1080, 1937.
- ²⁸ Tuell, J. I.: Vitallium in Internal Fixation in Bone Surgery. Northwest Med., 39, 163-165, 1940.
- ²⁹ Venable, C. S., Stuck, W. G., and Beach, A.: The Effects on Bone of the Presence of Metals: Based Upon Electrolysis. ANNALS OF SURGERY, 105, 917-938, 1937.
- ³⁰ Venable, C. S., and Stuck, W. G.: Electrolysis Controlling Factor in the Use of Metals in Treating Fractures. J. A. M. A., 111, 1349-1352, 1938; *idem*: Recent Advances in Fracture Treatment with Nonelectrolytic Metal Appliances. Jour. Ind. Med. Assn., 31, 335-342, 1938; *idem*: Vitallium Nails in Fracture of the Hip. Surg., Gynec. and Obst., 70, 964-968, 1940; *idem*: The Use of Vitallium Appliances in Compound Fractures. Amer. Jour. Surg., 51, 757-766, 1941; *idem*: Three Years' Experience With Vitallium in Bone Surgery. ANNALS OF SURGERY, 114, 309-315, 1941; *idem*: A General Consideration of Metals for Buried Appliances in Surgery. Surg., Gynec. and Obst., 76, 297-304, 1943.

BRIEF COMMUNICATIONS

TRANSPLANTATION OF THE PERITONEUM DURING SUPRAPUBIC CYSTOTOMY

ROBERT L. PAYNE, M.D.
NORFOLK, VIRGINIA

SUPRAPUBIC CYSTOTOMY is both an urgent and necessary procedure under many conditions. A second suprapubic cystotomy following a previous one is also a frequent necessity. It is during the effort to perform a secondary

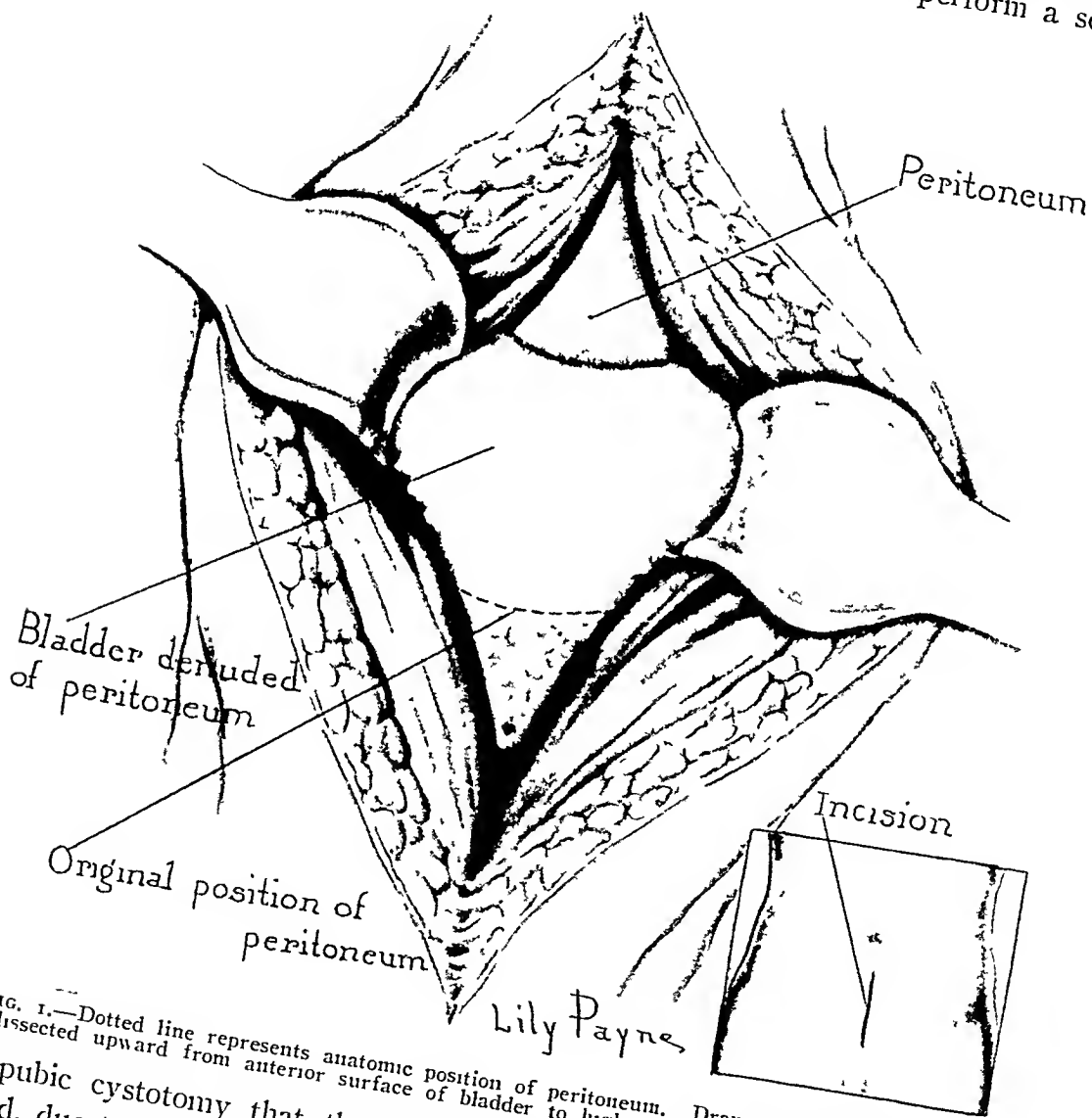


FIG. 1.—Dotted line represents anatomic position of peritoneum. Drawing shows peritoneum has been dissected upward from anterior surface of bladder to highest point possible on dome. suprapubic cystotomy that the peritoneum over the bladder is frequently opened, due to the adhesive confluence of the layers of the abdominal wall. Following the first suprapubic cystotomy, if the peritoneum is opened, usually dirty, infected urine from the bladder is extravasated into the peri-

toneal cavity, which, in many instances, results in the serious complications of peritonitis. Frequently a small rent is made at the time of the second suprapubic opening of the bladder without the knowledge of the surgeon, and rather large amounts of infected urine escape into the peritoneal cavity.

To prevent this complication of peritoneal contamination by urine, I have been transplanting the peritoneum, as a routine, in every primary supra-

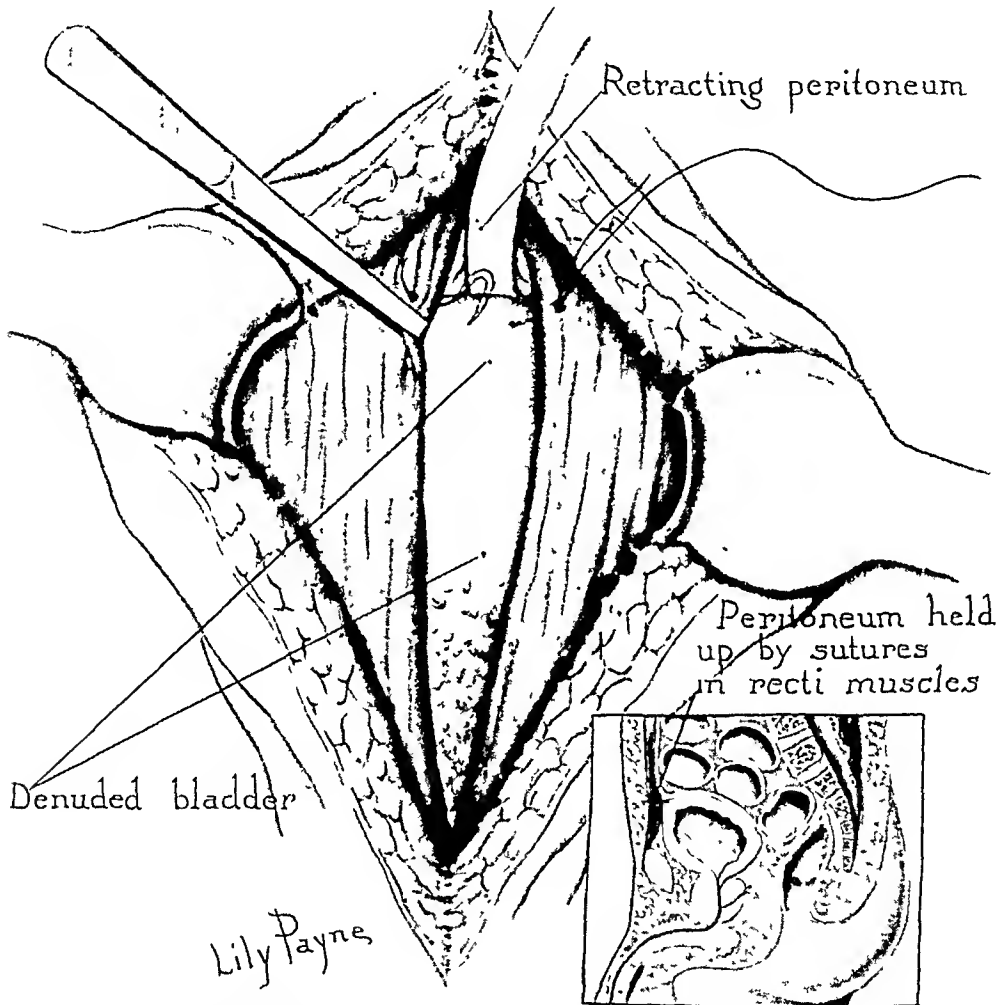


FIG. 2.—Peritoneum fixed in position of high transplantation by one or more sutures placed through rectus sheath and bladder wall.

pubic cystotomy for the past 25 years. I have experienced a great deal of satisfaction and comfort from the procedure herein described of permanently transplanting the peritoneum high up and well back on the dome of the bladder, thus eliminating the possibility of tearing into the peritoneum when opening the bladder again, following a previous suprapubic cystotomy. The illustrations show that the first step, after the bladder is exposed, is to strip the peritoneal reflexion, over the bladder, upward as high as possible, and maintaining the peritoneum in this transplanted position by suturing the rectus fascia and sheath to the bladder at the highest point in the wound.

TRANSPLANTATION OF PERITONEUM

This not only provides a wide area of the anterior surface of the bladder, through which the opening in the bladder is made, but also prevents the peritoneal reflexion from subsequently rolling downward and becoming adherent in the lower region of the incisional approach to the bladder. Thus, in doing any subsequent suprapubic cystotomy, the danger of opening the peritoneum is eliminated, and one can approach the bladder at the secondary cystotomy through the old incision and through the anterior bladder wall with confidence against peritoneal contamination by infected urine. Over a period of years, I have observed a few fatal instances of peritonitis due to urinary extravasation into the peritoneal cavity following a secondary suprapubic cystotomy. It is often necessary to open the bladder a second time by suprapubic approach for recurring tumors, incompletely removed, solitary ulcers, recurring stones, diverticula, and last, but not least, the day has not passed when suprapubic prostatectomy in two stages may be the method of choice for hypertrophy of the prostate.

The procedure herein described is probably being utilized by many surgeons, and I know of a good many who have adopted this procedure after it was demonstrated to them by me. Since I have never seen this maneuver described in literature, I am submitting it for what possible good may accrue therefrom.

TRANSVERSE MEGACOLON ASSOCIATED WITH CHRONIC VOLVULUS

CASE REPORT

LOUIS P. RIVER, MAJOR, M. C.

FORT WORTH, TEXAS

AND

JOHN A. GUBLER, LT., M. C., U.S.N.R.

NORFOLK, VIRGINIA

FROM THE DEPARTMENT OF SURGERY, LOYOLA UNIVERSITY COLLEGE OF MEDICINE, AND THE COOK COUNTY HOSPITAL, CHICAGO, ILL.

FEW CASES of congenital or adult megacolon limited to the transverse colon have been reported.¹ We have been unable to find recorded in the literature any case of chronic volvulus of such a megacolon. Striking parallelism exists, as might be expected, between the history, symptoms and findings in the case herewith presented and similar lesions of the cecum and sigmoid.

In a communication on volvulus of the cecum, River and Reed² described recurrent obstructive episodes, characterized by slow progress, diffuse colic and tenderness, marked tolerance by the patient to the incomplete obstruction and great distention, and late vascular damage. Similar observations have been made regarding recurrent or chronic volvulus of the sigmoid, almost habitually associated with megacolon of that segment.^{3, 4, 5} In both diseases the dilatation and hypertrophy of the involved segment is evidence of a long-continued physiologic maladjustment, of which extrinsic causes such as cathartic habituation must be distinctly secondary. Anatomic variations such as hypo- and hyperfixation provide the opportunity for kinking. Obviously, it is impossible from this case to adduce evidence for other possible intrinsic etiologic factors, or to say whether the elongated thickened mesocolon or the heavy, hypertrophied transverse colon was primary. No organic obstruction was found at the splenic flexure.

The enormous abdominal distention and respiratory distress seen in our patient agree with the conditions present in sigmoid volvulus. The radiation of pain into the right flank was probably because of pull on the parietal peritoneum at the hepatic flexure and distention of the proximal ascending colon. The pain in the right shoulder and down the arm was apparently the result of diaphragmatic irritation from the enormous pneumoperitoneum due to intermittent leakage through multiple small perforations. We are unable to explain how this happened without gross peritoneal contamination. About nine months elapsed between the first and second attacks observed by us, although the patient said that he had had them as often as once a month.

Case Report.—J. V., white, male, age 58, a street car motorman, was admitted to Cook County Hospital at 10:35 A.M., July 21, 1941, with a diagnosis of acute intestinal obstruction. He complained of abdominal pain and distention beginning 18 hours previously, but stated he had had intermittent attacks of cramping pain at progressively

MEGACOLON WITH VOLVULUS

shorter intervals for ten years, in which epigastric colicky pain radiated to the right flank, constipation was marked, but nausea or vomiting did not occur. With frequent attacks during the past few months he had noted acute, steady pain radiating to his right shoulder and arm. The onset of the present episode was sudden, violent, with severe steady pain in the upper abdomen, mild nausea, but no vomiting. He was



FIG. 1.—Appearance on admission, July 21, 1941

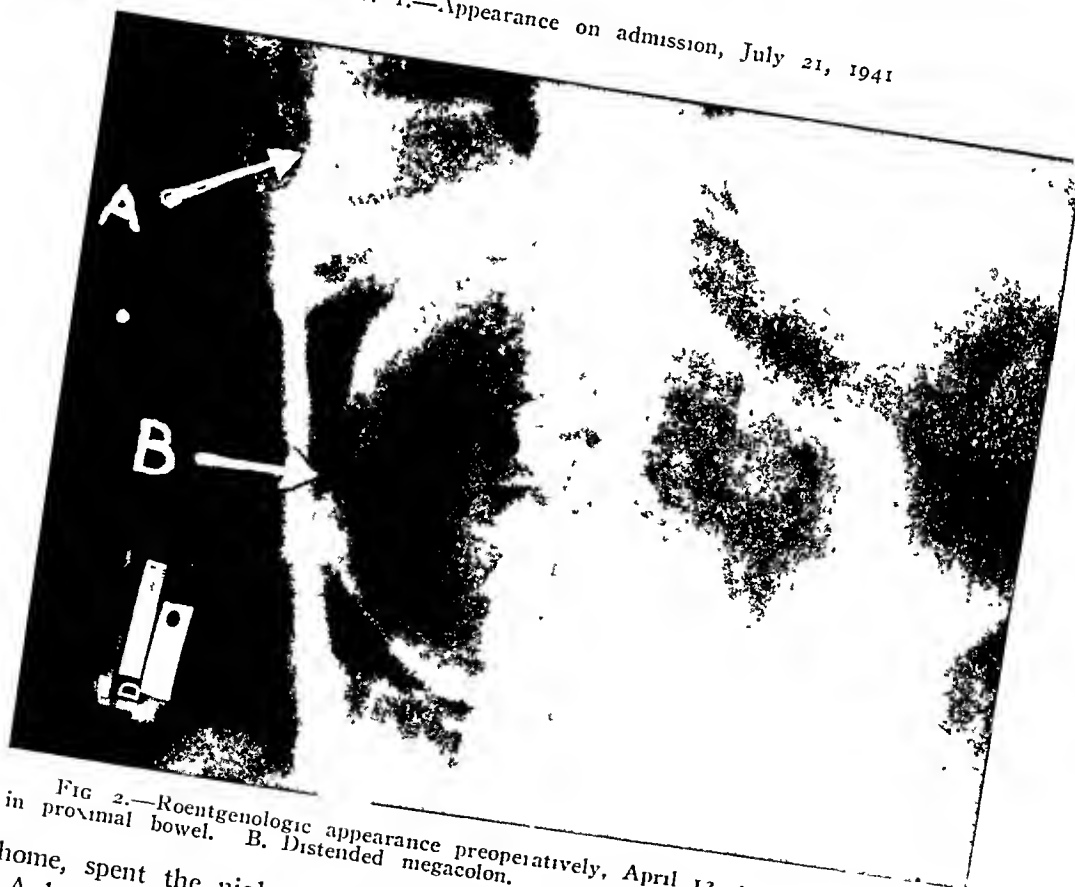


FIG. 2.—Roentgenologic appearance preoperatively, April 12, 1942. A. Distention in proximal bowel. B. Distended megacolon.

taken home, spent the night in great discomfort, occasionally passing flatus, without relief. A large soft bowel movement before admission relieved him somewhat, but he began to note more severe shoulder and arm pain. He gave no history of selective dyspepsia, had been jaundiced mildly ten years ago, said he had had dyspnea lately with attacks. He had controlled a mild diabetes by diet for ten years, discovered when he had a tonsillectomy performed.

Physical Examination.—The patient was a large, obese male (240 lbs.), lying quietly in bed, not seeming acutely ill, with a barrel-like emphysematous chest and enormous soft tympanitic distention of the abdomen (Fig. 1). (The apex of the abdomen was 42 cm. above the table). There were inconstant moist râles at both bases posteriorly. The liver was felt three fingersbreadth below the costal margin; there was direct and rebound tenderness in the epigastrium, no rigidity, masses, scars or herniae. There was moderate periumbilical venous dilatation and engorgement of numerous small veins on the abdomen. Tinkling, high-pitched bowel sounds, 5-10 per minute, not coincident with pain, were heard.

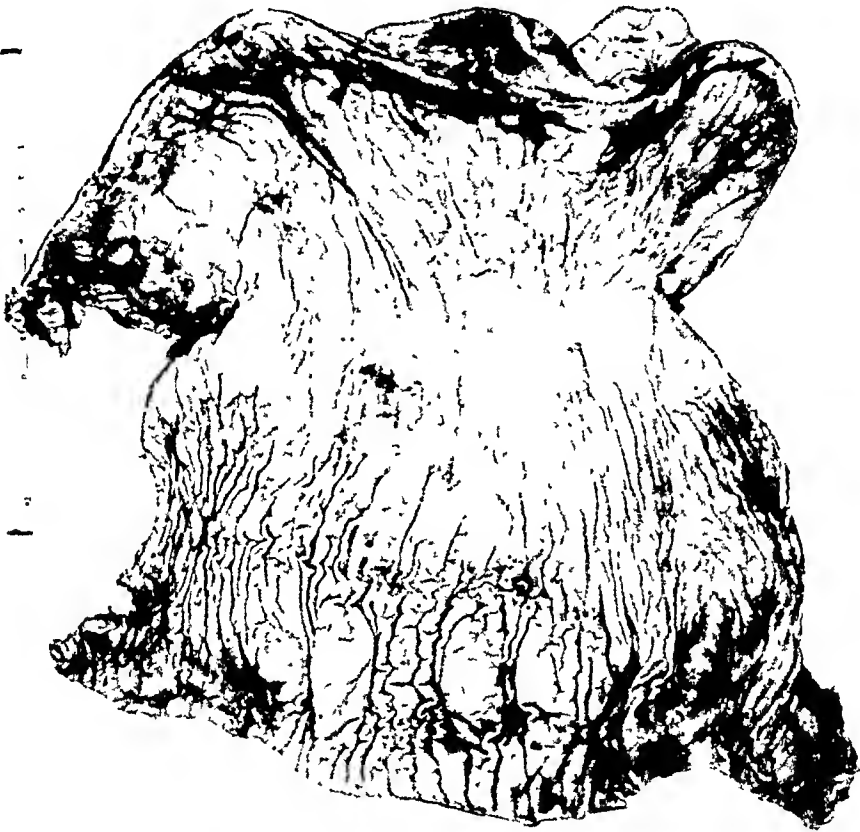


FIG. 3.—Rule is 15 cm. Mucosal aspect. Bowel is opened along mesenteric border in long axis

The white blood count was 8,500; the urine negative; blood sugar 150 mg. per cent, and icterus index 21. Fifteen hundred cubic centimeters of a two-quart enema were returned highly colored. He was given mineral oil and enemata every two hours. Oil came through in four hours, but the distention became greater. The roentgenologic appearance was almost identical with that seen in Figure 2, and was interpreted by the junior author as volvulus in a Hirschsprung's disease. He continued to pass oil, his tenderness decreased although the distention did not. Seventy-two hours after admission he was given 150 mg. of procaine intrathecally, and passed 5,500 cc. of liquid stool, with large amount of gas. His abdomen flattened out. One week later he left the hospital apparently well.

He was readmitted, April 12, 1942, at 3:55 P.M., six hours after a "normal" bowel movement. He had had increasing distention and diffuse aching pain for three days. The onset had been insidious; dyspnea and right shoulder pain had been severe; he

MEGACOLON WITH VOLVULUS

had no appetite, but had no nausea or vomiting. There was diffuse direct tenderness, extreme tympany. The abdomen was silent. The appearance was the same as before. The roentgenographic appearance, shown in Figure 2, led to a diagnosis of volvulus of the transverse colon. The film was not large enough to show the diaphragmatic region, where the enormous pneumoperitoneum was evident. At 11:20 P.M. he was given 110 mg. of metycaine intrathecally. No evacuation occurred.

Operation.—Through a left paramedian incision, a large amount of odorless air escaped upon incision of the peritoneum. There was an enormous megacolon of the transverse colon, with a 180° counterclockwise volvulus, the proximal portion of bowel (Fig. 2 A) passing behind the distal portion. The wall of the involved colon was thick, leathery and covered with multiple pebbly, verrucous areas, also patches of plastic

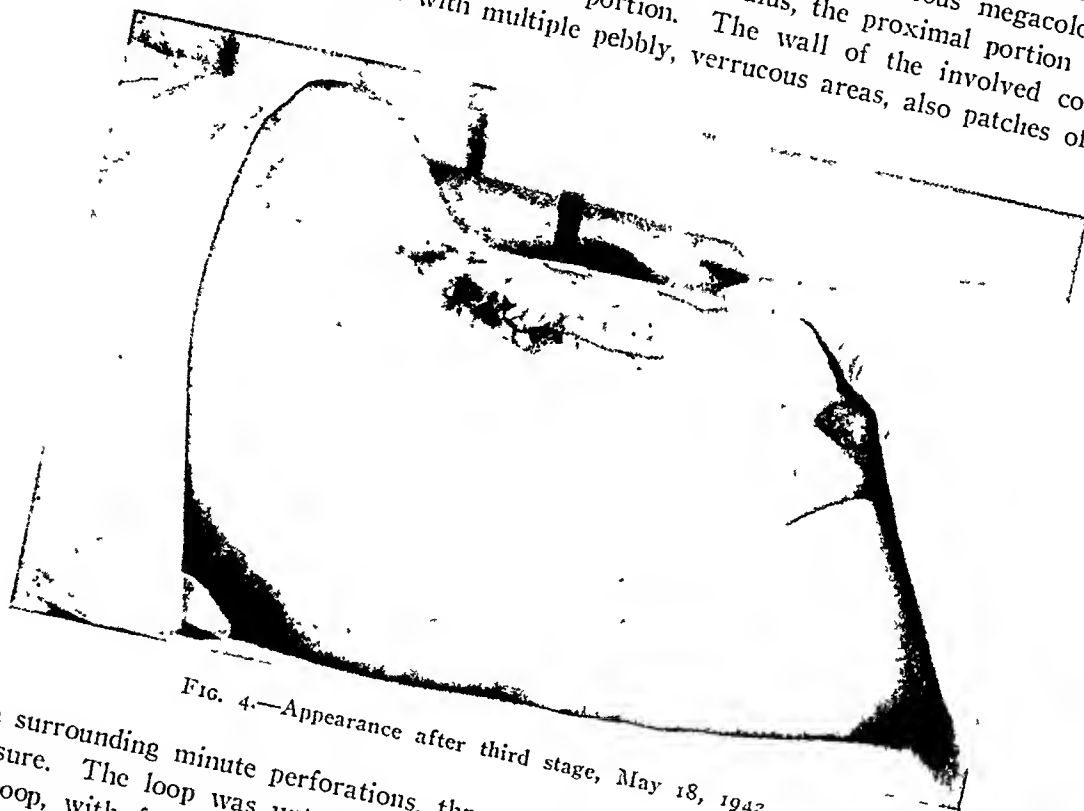


FIG. 4.—Appearance after third stage, May 18, 1942.

exudate surrounding minute perforations, through which small quantities of air escaped on pressure. The loop was untwisted; the mesentery was thick, elongated. Pressure on the loop, with four rectal tubes in place, failed to reduce the tumor appreciably. It was exteriorized, the wound closed and a large catheter purse-stringed into the loop. During the next ten days bowel sounds became normal, his general condition improved and, on April 24, 1942, the exteriorized mass was resected with the cautery, carefully avoiding damage to mesocolic vessels. The posterior bowel surfaces were sutured leaving a saucer-like defect. Figure 3 shows the resected specimen, opened. The abdomen was scaphoid.

On May 18, 1942 the skin edges were freed, the circumference of the bowel restored by layer closure and the skin closed. No attempt was made to repair the hernia which existed (Fig. 4). There was gradual improvement in the amount of leakage and he was discharged, July 1, 1942, having normal stools, no abdominal pain, and no difficulty from a 4 x 5 cm. hernial defect.

Pathologic Report: A segment of large bowel measuring 27 cm. in length. The wall is 12 mm. thick. The serosal surface is granular, purple-gray and tan. There is marked hypertrophy of muscular elements. The mucosa is gray-tan covered with bloody mucus. In one area are defects one and two millimeters in diameter communicating with the serosal surface. There is a serosal peritonitis.

SUMMARY

1. Associated megacolon and volvulus of the transverse colon is compared with similar lesions of sigmoid and cecum.
2. A case is reported demonstrating the recurrent or chronic character of this previously unreported lesion.
3. The diagnostic importance of plain films of the abdomen is emphasized.

REFERENCES

- ¹ Krombach, K.: Case of Congenital Transverse Megacolon. *Monatschrift fur Kinderheilkunde*, 38, 190, Jan.-Feb., 1928.
- ² River, Louis., and Reed, Francis A.: Volvulus of the Cecum. *ANNALS OF SURGERY*, 116, 874-881, December, 1942.
- ³ Cope, Zachary: *The Early Diagnosis of the Acute Abdomen*. Oxford Medical Publications, 6th Ed., 1932.
- ⁴ Edwards, Scott R.: Megacolon Associated with Chronic Volvulus of the Sigmoid. *Indianapolis Med. Jour.*, 24, 139-143, June, 1921.
- ⁵ Ligat, D., and Overend, T. D.: Recurrent Volvulus of the Pelvic Colon. *Brit. Med. Jour.*, 3782, 7-12, July 1, 1933.

ANEURYSM OF THE BRACHIAL ARTERY

REPORT OF SUCCESSFUL ANEURYSMORRAPHY

JOHN P. BRUCKNER, M. D.
NEW YORK, N. Y.

FROM THE SURGICAL SERVICE OF HARLEM HOSPITAL, CLARENCE P. HOWLEY, M.D., DIRECTOR, NEW YORK, N. Y.

TRAUMATIC ANEURYSM of the brachial artery occasionally occurs, and gives rise to disability from enlargement and pressure upon the median and ulnar nerves. Such an aneurysm has arisen as a result of injury to the vessel wall by knife wound, destroying the media but leaving the intima intact. The following case report illustrates the sequence of events occasioned by the gradual enlargement of an aneurysmal sac to the point of producing changes in the nerves to the forearm:

Case Report.—A. L. was admitted to the hospital, May 2, 1942, for a severe knife wound of the midportion of the anterior surface of the right arm. The wound was about five inches long and penetrated the belly of the biceps brachii muscle and injured the outer layers of the brachial artery at the junction of the middle and upper third. Immediate operation consisted of débridement and suture repair of lacerated sutures. The brachial artery was not sutured. Recovery was uneventful, and the patient was discharged on the eighth day postoperative.

On June 29, 1942, he was readmitted for marked swelling in the midportion of the right arm, with sensory disturbances to the forearm, hand and fingers, over the area of the median and ulnar nerve distribution. A diagnosis of aneurysm of the brachial artery following injury was made, and a plan outlined to establish the relationship of the aneurysm and diodrast injected into the tumor. Roentgenograms were immediately taken. The tourniquets were removed, and two days later a tourniquet was applied to the arm proximal to the aneurysm and diodrast injected into the median basilic vein. Another roentgenogram was taken and compared with that previously taken for evidence of arteriovenous relationship. No arterial and venous communication was noted. However, further study was made to ascertain the aneurysm involved the power of the venous blood of both forearms. In the specimen from the left forearm the CO₂ combining power was 54 vol. per cent; in that from the right forearm, 52 vol. per cent. From these observations, it seemed logical that the aneurysm involved the brachial artery alone. The tissues surrounding the aneurysm were very tense, which could not be palpated. The injection of diodrast revealed a bruit. Following the injection of diodrast and application of tourniquets the arm rapidly increased in size, apparently from extravasation of blood through the needle puncture wound. The blood Kahn was negative.

Operation.—July 8, 1942: An incision was made over the brachial artery proximal to the sac and the brachial artery dissected free from its position between the median and ulnar nerves. A traction tape was applied around the artery for compression when needed. The incision was then enlarged downward over the sac to about 2 cm. distal to the sac and the skin flaps dissected free on either side for a distance of one inch. The sac ruptured spontaneously at this point, expelling bright red arterial blood and a few dark red blood clots. Bleeding was controlled by compression of the artery with the tape pre-

viously applied and by digital pressure over the openings within the sac. A soft rubber, No. 8 F. catheter, coated with vaseline, was inserted into the arterial lumen within the sac. Three layers of Lembert sutures of No. 0 chromic catgut through the walls of the sac, after the manner of Matas' aneurysmorrhaphy, were applied and the catheter withdrawn. Pulsation of the radial artery at the wrist became full and bounding. The remaining portion of the sac was dissected free and removed. The traction tape surrounding the brachial artery was withdrawn. The deep fascia was closed with continuous catgut sutures and the skin closed with interrupted silk without drainage.

Recovery was uneventful except for a wound infection which was opened on the eighth postoperative day by removal of the sutures. The patient was discharged from the hospital, July 22, 1942, at which time the motor function of the right arm, forearm, and hand was good and the slight sensory loss over the median and ulnar nerve areas previously noted had disappeared.

The patient was again seen, December 18, 1942, and the following notation made: "Function of the forearm, hand and fingers, not restricted. Radial pulsation at the wrist, good. No sensory or motor disturbances found. Wound healed. No evidence of recurrence of aneurysm."

COMMENT.—Aneurysmorrhaphy, as described by Matas, Bernheim, and others, appeared to offer desirable therapy in this instance since the aneurysm was considered to have been produced following an injury to the arterial wall.

The development of sensory disturbances along the median and ulnar nerves, together with swelling of the hand and fingers resulting from pressure effects upon the return flow of lymph, and the compression of the brachial vein, were indications for operative intervention.

A significant incident of noteworthy interest was the freedom from serious complications that might have been expected from infection in an operative wound of this nature. Aside from induration and swelling of the tissues along the incision, which rapidly subsided with the free outlet of pus, complete recovery and restoration of function was uneventful. Chemotherapy was not employed, and was considered unnecessary, since drainage was adequate.

TRAUMATIC ARTERIOSCLEROTIC ANEURYSM OF THE TIBIAL ARTERY SIMULATING AN OSTEOGENIC SARCOMA OF THE FIBULA

CASE REPORT

JACK D. KIRSHBAUM, M.S., M.D., AND GEORGE L. KRAFT, M.D.
MAJOR, M.C. CHICAGO, ILL. LI. U. S. N.

FROM THE DEPARTMENT OF PATHOLOGY, WOODLAWN HOSPITAL, AND THE ORTHOPEDIC SERVICE OF DR. PHILIP LEWIN, COOK COUNTY HOSPITAL, CHICAGO, ILL.

THE ABILITY of aneurysms of the aorta to erode bone, particularly the vertebra or ribs, is well known, and observed rather frequently. That a traumatic aneurysm of the anterior tibial artery should have assumed such large proportions so as to destroy the upper end of the fibula and clinically manifest itself as a bone sarcoma, is certainly most unusual.

Case Report.—The patient, a white female, age 52, was admitted to the Medical Service, Cook County Hospital, March 22, 1938, with gastro-intestinal complaints. Because of the presence of a large mass in the right leg she was then transferred to the Orthopedic Service. She stated that in February, 1937, she had fallen off a street car. Three months later pain occurred in the lateral aspect of the right leg. The leg

FIG. 1.

FIG. 2.

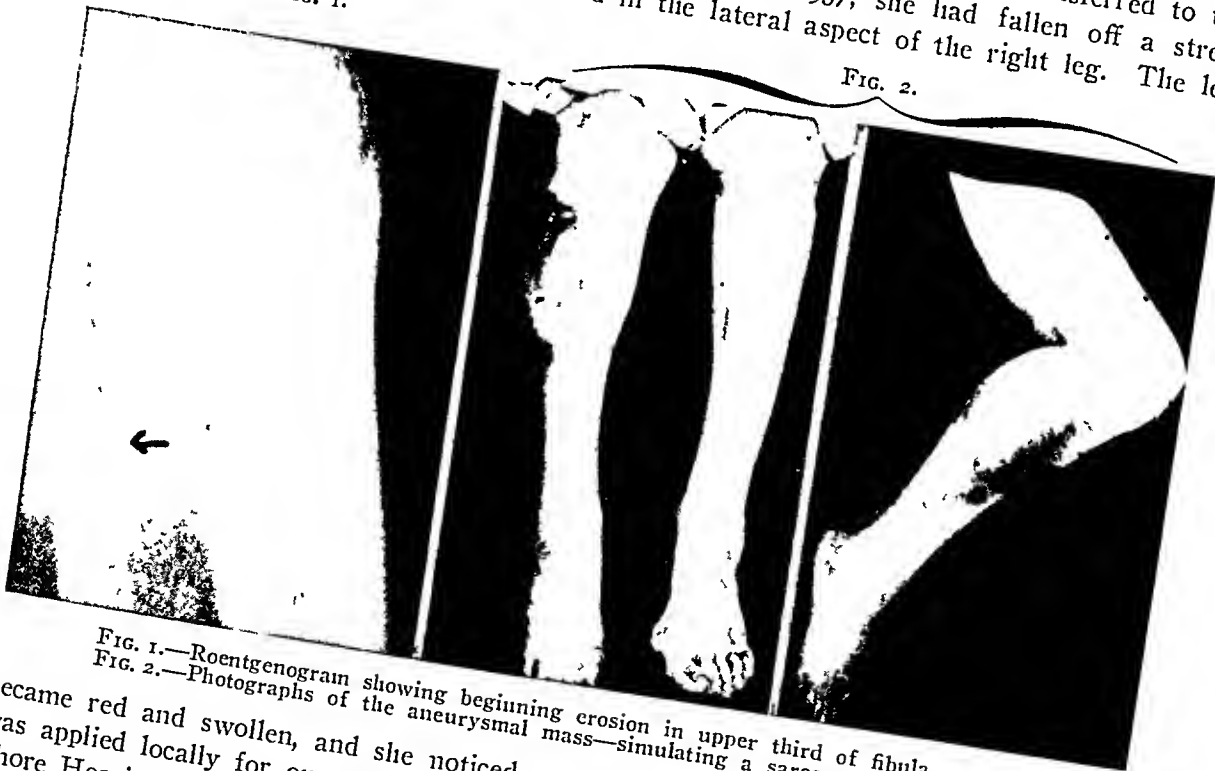


FIG. 1.—Roentgenogram showing beginning erosion in upper third of fibula.
FIG. 2.—Photographs of the aneurysmal mass—simulating a sarcoma.

became red and swollen, and she noticed a small pimple just below the knee. Heat was applied locally for one month. In October, 1938, she was admitted to the South Shore Hospital. A swelling was present in the upper third of the lateral aspect of the right leg. It was excruciatingly tender, and felt fluctuant. The ankles were edematous. A diagnosis of osteomyelitis of the upper third of the tibia, with a subperiosteal abscess, was made. Roentgenograms disclosed slight involvement of the periosteum in the upper end of the right fibula (Fig. 1). The tibia was negative. For the past 15 years the

patient had noticed marked dyspnea on exertion and had been told she had heart trouble. No history of rheumatic fever was obtainable. The urine contained much albumin. R.B.C. 3,100,000.

The swelling was incised, and a dark, bloody material was obtained. The swelling reoccurred and nothing was done until she entered the Cook County Hospital in March, 1938. Physical examination disclosed a large fluctuating mass, the size of a grapefruit, in the outer and upper third of the right fibula. The mass was tender, fluctuant in the center and indurated at the periphery. The overlying skin was dis-

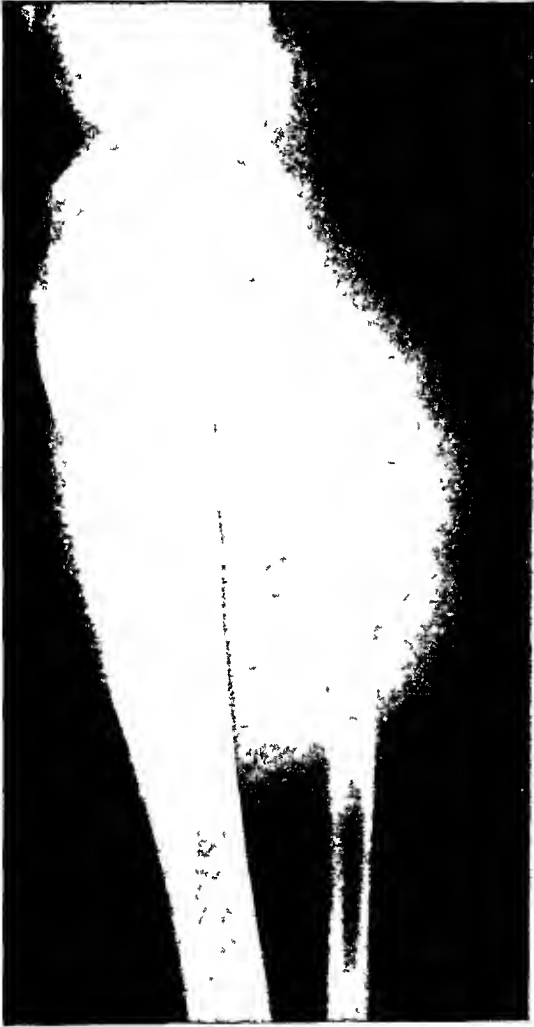


FIG. 3.—Roentgenogram showing the large soft-tissue mass and destruction of the upper end of the fibula.



FIG. 4.—Photograph of the excised aneurysm filled with a laminated hematoma.

colored a coppery-brown, which faded towards the periphery, and the central part was covered over by a thick adherent scale. The superficial veins in the skin were very prominent (Fig. 2). Temperature 97.8° F.; pulse 100; respirations 24; blood pressure 126/88. Except for a slight enlargement of the heart, the remaining findings were irrelevant. *Laboratory Data:* Urinalysis showed albumin 2 plus, spr. gr. 1.008, sugar negative. Blood: Hb. 60%; W. B. C. 4,400. Blood Wassermann negative. *Clinical Impression:* Osteolytic sarcoma of the fibula and auricular fibrillation.

Roentgenologic examination of the right leg disclosed complete destruction of the upper end of the fibula and a marked soft-tissue swelling of the upper end of the tibia (Fig. 3).

TRAUMATIC ANEURYSM

Subsequent Course: In view of the patients gastro-intestinal complaints, and loss of weight, the lesion in the leg was considered a metastasis. However, roentgenologic studies of the gastro-intestinal tract and chest were all negative. A biopsy taken from the mass disclosed only necrotic tissue. While in the ward the patient developed signs of uremia. Blood chemistry revealed a urea nitrogen of 57.44 mg., and creatinine of 3.74 mg. Although a diagnosis of sarcoma of the fibula was considered, amputation of the leg was thought inadvisable. The condition of the patient became poorer and she expired three months after admission, 15 months following her accident.

Necropsy: The autopsy was restricted to examination of the right lower extremity. The body was that of a fairly well nourished white female. Over the right medial condyle of the femur there was a light purple patch, 20 mm. in diameter. There was a

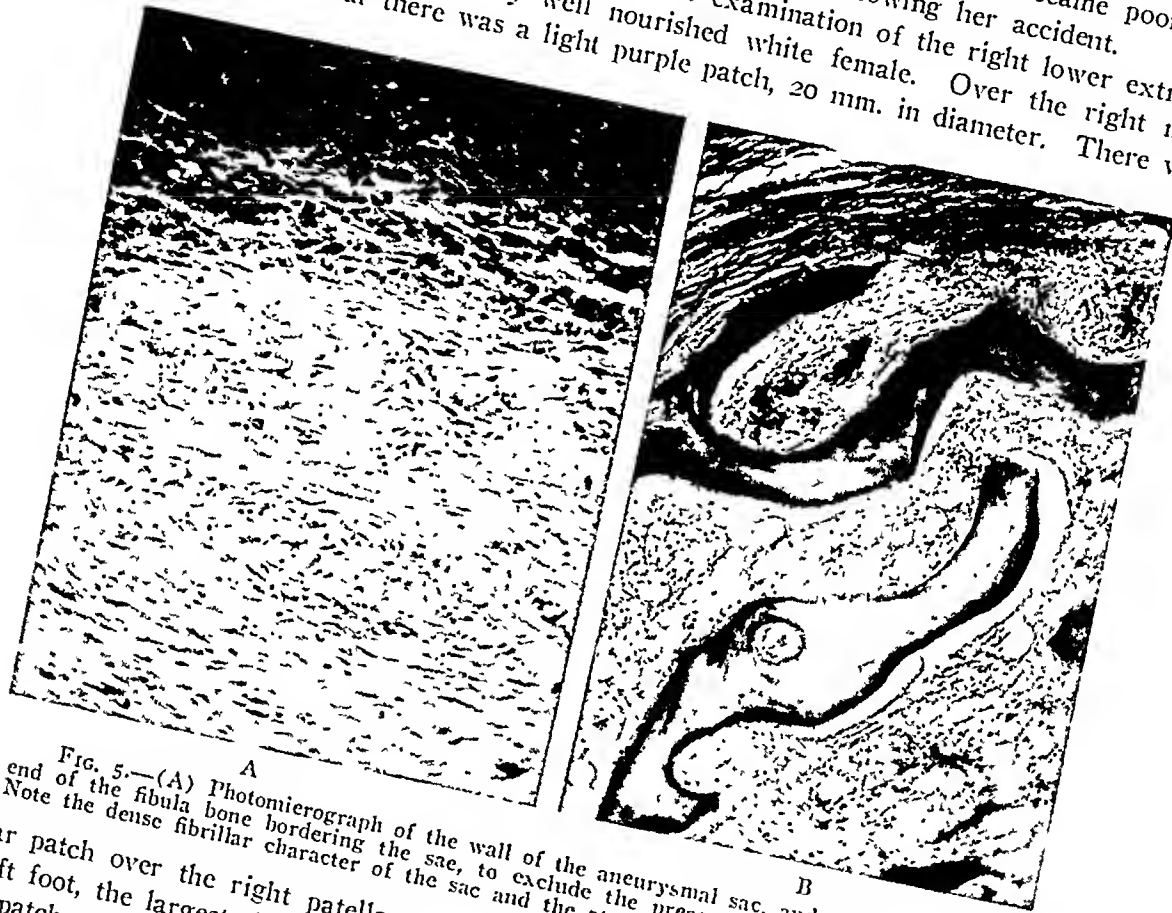


Fig. 5.—(A) Photomicrograph of the wall of the aneurysmal sac, and, also, (B) of the end of the fibula bone bordering the sac, to exclude the presence of a malignant tumor. Note the dense fibrillar character of the sac and the atrophic spicules of bone.

similar patch over the right patella, and four such patches on the plantar surface of the left foot, the largest, four centimeters, in the region of the heel. There were two other patches, over the right lateral malleolus and on the medial aspect of the heel. The upper two-thirds of the right leg was transformed by a tumor mass, measuring 40 cm. in transverse and 15 cm. in longitudinal diameter. The skin over the lateral aspect of the mass was deeply pigmented and contained a healed scar, four centimeters long. The muscle, in the vicinity of the above described mass, was friable, and in places was replaced by a reddish-brown tissue. On sectioning, the mass was found to be composed of an organized and laminated blood clot (Fig. 4). The inner lining of the sac was fairly smooth and discolored purple-grey. The fibula in the upper third was missing. The end of the bone was roughened and sharply demarcated from the sac. Bordering the sac it was noted to communicate with the anterior tibial artery.

Pathologic Examination.—Microscopic: The sac is lined by a thick layer of red blood cells and fibrin, which rests upon a thick, slightly vascular granulation tissue infiltrated with plasma cells, round cells and an occasional multinucleated giant cell (Fig. 5). There are large numbers of histocytes filled with golden-brown pigment. The wall of the sac, in places, also shows calcification. Bordering this sac there is a large branch of the anterior tibial artery showing a marked calcification of the media,

thickening of the intima, and the lumen partially filled by a recent blood clot. The adventitia is heavily surrounded by large numbers of polymorphonuclear leukocytes, round cells, and eosinophil leukocytes. The elastic stain shows a gap in the wall of the artery and partial replacement by scar tissue, and thus permits free communication between the lumen of the vessel and the aneurysmal sac. In the lumen of the vessel is an organizing small piece of thrombus (Fig. 6). The fibula fragments of bone adjacent to the sac shows widely separated atrophic spicules. The bone marrow is fatty (Fig. 5B). There are no evidences of syphilis or malignancy in the numerous sections taken. *Anatomic Diagnosis:* Arteriosclerotic traumatic aneurysm of the anterior tibial artery and erosion of the upper third of the fibula. Hypertensive heart disease with renal decompensation (clinically) and multiple hemangioma of the skin.

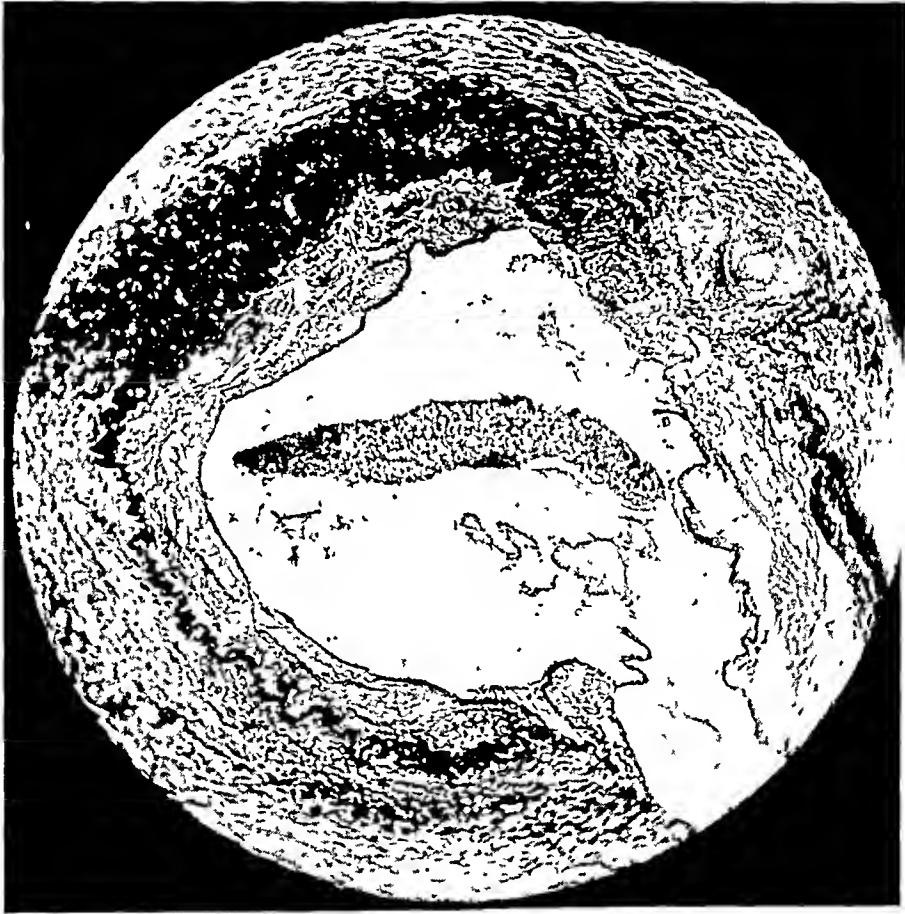


FIG. 6.—Photomicrograph showing the large defect in the wall of the tibial artery. Note the marked sclerosis of the media and the thrombus in the lumen.

Discussion.—There are so-called aneurysms of the bone which are usually located at the ends of the long bones and are called by Ewing¹ telangiectatic sarcomata. These tumors are composed of large vascular spaces and show invasive malignant features. Another type of aneurysm of the bone may be due to the degeneration of a giant cell tumor which permits blood to flow through the large central spaces. These lesions are not aneurysms in the strict sense of the word, since there is not a rupture of the layers of a blood vessel. The true aneurysm shows a rupture in the adventitia, or adventitia

TRAUMATIC ANEURYSM

and media layers, permitting a weakening of the wall so that distension occurs and may eventually rupture.

A false aneurysm may result from a traumatic rupture of a vessel wall and the subsequent formation of an encapsulated hematoma communicating with the original vessel (Karsner²). The case cited illustrates the formation of a huge aneurysm in an arteriosclerotic blood vessel, following a trauma to the leg, with erosion of the upper end of the fibula bone.

SUMMARY

A case of a false arteriosclerotic traumatic aneurysm of the tibial artery with marked destruction of the fibula bone is here presented.
The aneurysm clinically was mistaken for an osteogenic sarcoma.

REFERENCES

- ¹ Ewing, James: *Neoplastic Diseases*. 4th Ed., W. B. Saunders, p. 361, 1940.
- ² Karsner, H. T.: *Human Pathology*. 5th Ed., J. B. Lippincott Co., p. 902, 1938.

A METHOD OF PROLONGED VENTRICULAR DRAINAGE

ALBERT S. CRAWFORD, M.D.* AND RALPH A. MUNSLOW, M.D.*

DETROIT, MICH.

OCCASIONALLY it becomes necessary to establish ventricular drainage for a number of days or even several weeks. In such cases the greatest risk is of infection. This latter is most likely carried in along the catheter when it has to be manipulated because of stoppage of flow.

FIG. 1.

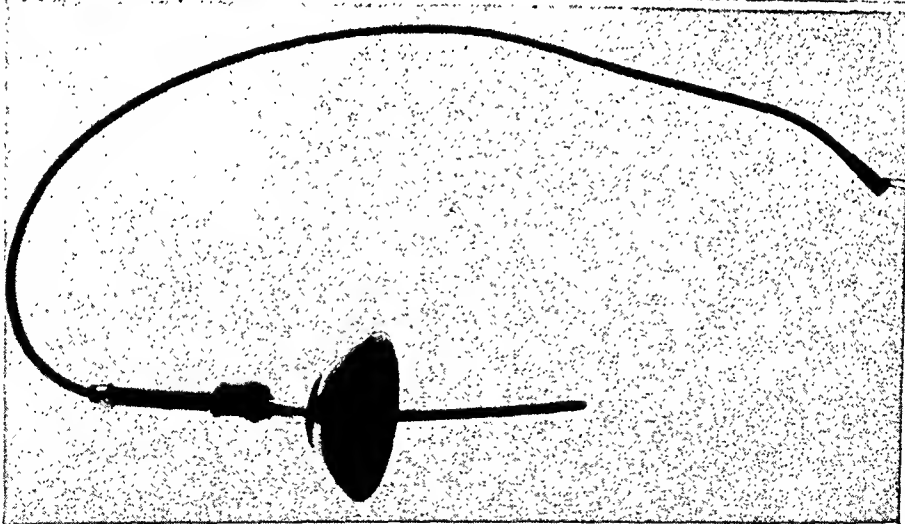


FIG. 2.

FIG. 1.—Shows the apparatus on a boy of 11, with an unremovable midline glioma of the cerebellum. The drainage was continued until the deep X-ray therapy was completed.

FIG. 2.—Shows the catheter and retaining-protecting apparatus assembled. Details are given in the text.

* Albert S. Crawford, Division of Neurologic Surgery, Henry Ford Hospital, Detroit, Mich. Ralph A. Munslow, now Captain U. S. Army Medical Corps.

PROLONGED VENTRICULAR DRAINAGE

For a number of years we have used the well known drainage system, pictured here (Fig. 1), which uses an inverted Y-tube to break the suction effect of a column of water. As is known, the resistance to the outflow can be modified by varying the height of the Y-tube above the level of the trephine hole.

The chief difficulty in the method was occasional stoppage of flow, from one cause or another. This problem was solved partly by cutting two or three extra eyes in the inner end of the catheter.

In order to make it somewhat safer against infection, if manipulation of the catheter should become necessary, we added the apparatus herewith pictured (Fig. 2). It consists of an ordinary rubber vacuum cup attached to an enveloping tube by a short glass nipple which has flanges blown at each end. We use a No. 8 French rubber catheter to insert into the ventricle. It can be passed down the pathway made by an ordinary large brain trocar, if the hole in the dura is made slightly larger before the insertion. The enveloping tube is made by cutting off the upper 4.5 or 5 cm. of a size No. 16 F. catheter. The enlarged end slips over the flanged end of the glass nipple. An ordinary Michel clip serves to constrict the outer end of the enveloping tube down, so that it grips the inner catheter snugly. It is safer, however, to also secure it with a piece of thread, fastened on the scalp with three or four silk sutures. If desired, some sulfanilamide, or similar powder, can be used under the rubber cup around the catheter; however, this will cake in a place. Silk ties make all joints of the tubing more secure.

Inasmuch as the whole apparatus is sterilized before assembling, it gives one a closed sterile system which permits, if necessary, of manipulation of the catheter without disturbing the dressings and with less danger of carrying infection inwards with the catheter. One must be sure that the down tube to the collecting bottle is not too long or that it does not become kinked, as there will result a backing up of fluid.

Of course, no method is foolproof. No drainage should be left longer than necessary. We have found this method definitely superior to the other methods we have tried for prolonged ventricular drainage.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.

BOOK REVIEW

YEARBOOK OF INDUSTRIAL AND ORTHOPEDIC SURGERY. Edited by Charles F. Painter. M.D. Yearbook Publishers, 424 pp., 302 ills., \$3.00, Chicago, 1942.

This compact and well illustrated edition deals almost entirely with orthopedic problems. Most of the articles are well summarized and the operative technic are fully described. The articles on acute hematogenous osteomyelitis emphasize the success of conservative nonoperative therapy using sulfonamides and adequate plaster immobilization. The therapy of chronic arthritis is well represented. Of special interest is the large number of reviews dealing with minor disabling conditions of the shoulder girdle. More than one quarter of the book is given over to fractures and traumatic dislocations—the newest methods of treatment are described and illustrated. The section on industrial medicine and surgery has several reviews dealing with the general problems of industrial health. These are followed by articles discussing specific hazards in the various industries. Taken as a whole the book presents good summaries of the orthopedic and industrial health literature of the past year.

HENRY SALTONSTALL, M.D.

BOOKS RECEIVED

FRACTURES OF THE JAW BONES AND OTHER FACIAL BONES. By Glenn Major, B.S., A.M., Ph.D., D.D.S., M.D. St. Louis: C. V. Mosby Co., 1943.

ENDOSCOPIC PROSTATIC SURGERY. By Roger W. Barnes, M.S., M.D. St. Louis: C. V. Mosby Co., 1943.

OBSTETRICAL PRACTICE. By Alfred C. Beck, M.D. Baltimore: Williams & Wilkins Co., 1942.

THE SIGHT SAVER. By C. J. Gerling, A.B., M.A., B.C. New York: Harvest House, 1943.

THE PRINCIPLES AND PRACTICE OF WAR SURGERY. By J. Trueta, M.D. St. Louis: C. V. Mosby Co., 1943.

OPERATIVE ORAL SURGERY. 2nd Ed. By Leo Winter, D.D.S., M.D. St. Louis: C. V. Mosby Co., 1943.

BEHIND THE SULFA DRUGS. By Iago Gladston, M.D. New York: D. Appleton-Century Company, Inc., 1943.

OPERATING ROOM TECHNIQUES. By Edythe Louise Alexander, R.N. St. Louis: The C. V. Mosby Company, 1943.

ACUTE INFECTIONS OF THE MEDIASTINUM. By Harold Neuhof, M.D., and Edward E. Jemerin, M. D. Baltimore: The Williams & Wilkins Co., 1943.

NURSES IN ACTION. By Colonel Julia O. Flikke, A.N.C., A.U.S. Philadelphia: J. B. Lippincott Company, 1943.

DOCTOR IN THE MAKING. By Arthur W. Ham, M.B., and M. D. Salter, M.A., Ph.D. Philadelphia: J. B. Lippincott Company, 1943.



ANNOUNCEMENT

Announcement is made by the American Urologic Association that the annual prize of \$500 will not be awarded this year. Because of government restrictions on the holding of medical conventions except those primarily of military interest, the meeting of the American Urologic Association, which was to have been held in St. Louis, is cancelled.—Committee on Research, American Urologic Society.

ANNALS OF SURGERY

VOL. 117

JUNE, 1943

No. 6



MANAGEMENT OF THE COCOANUT GROVE BURNS

AT THE

MASSACHUSETTS GENERAL HOSPITAL



FOREWORD

ON Saturday evening, November 28, 1942, almost a year after America entered the war, a disastrous fire occurred in the Cocoanut Grove, a Boston night club. As a result, 491 people lost their lives and many were injured. Of the casualties, dead and living, 114 were brought to the Massachusetts General Hospital within a period of two hours. Had such a catastrophe taken place before Pearl Harbor, the hospital would have been swamped. As it was, the injured found the staff prepared, for the war had made us catastrophe-minded. The hospital was well prepared, partly as a result of the foresight of Dr. N. W. Faxon, Director, and of Dr. E. D. Churchill, Chief of the West Surgical Service, who had given careful thought to the problems of the hospital faced with a disaster; and partly to the good fortune that an active research program in burns was in progress at the hospital.

Early in 1942, two research projects were undertaken at this hospital under contract with the Office of Scientific Research and Development of the United States Government. One dealt with infections in compound wounds and burns, and the other with the physiology of burns. In both of these projects a number of the staff had taken part. All patients with burns, whether on the public or private wards, were used in the study. Modes of therapy were tried out and discussed at repeated staff conferences. A plan of therapy for burns, suited to use in a catastrophe, was developed and decided upon. When the victims of the Cocoanut Grove fire arrived, the treatment was ready and it was applied to all.

As in many disasters, the type of injury encountered in the casualties of the Cocoanut Grove fire conformed to a pattern. The lungs and airways were severely damaged, perhaps both by heat and irritating gases. The external burns were for the most part limited to skin surfaces not covered by clothing. Even the burns of eyes were of a pattern, the lower half of the

cornea of both eyes. In spite of the crowding and panic, there were no fractures.

The injury of the lungs presented the most pressing problem of therapy. The complications encountered were similar to those resulting from inhalation of certain war gases. They were also like those described following the disastrous fire at the Cleveland Clinic in 1929, believed due to toxic nitrogen gases released from burning roentgen films. This Cleveland disaster has come to be considered unique, for as a result of it the chemical content of roentgen film had been changed and all old film destroyed throughout the country. From the experience of the Cocoanut Grove fire, we know that such pulmonary complications are to be found not solely in warfare, but may be encountered at any moment in civilian life. The experience with these unusual lung complications is worthy of recording. Valuable material has been gathered dealing with the nature of the pathologic processes. The Massachusetts General Hospital and Harvard University have given unstintingly to insure a reaping of as much useful knowledge as possible.

The treatment used on the burns of the skin was unorthodox but the results were gratifying. Its simplicity has much to recommend it when large numbers of burns are encountered in a disaster. Because the method should prove of interest to the Armed Forces and to those charged with the responsibility of caring for civilian catastrophes, it deserves description particularly at this point of the World War.

The monograph has been arranged as a series of papers by the members of the staff who were responsible in their particular fields. The first three articles deal with the problems of administration and psychiatry peculiar to a civilian disaster. The next four recount the course and treatment of the lung injuries. The last five deal with the various aspects of the surface burns.

A brief protocol of each case, numbered consecutively, follows the last article. The same case numbers are used throughout all articles. Where cases are referred to and no details are given in the article, they are to be found in the protocol.

The authors dedicate this monograph to all those who labored with them yet remain anonymous, and to Dr. Churchill who guided us before he was called to serve in the Army.

OLIVER COPE, M.D.

The Massachusetts General Hospital acknowledges with gratitude the aid of the Josiah Macy, Jr. Foundation in sharing the cost of publication of the colored photographs.

THE PROBLEMS OF THE HOSPITAL ADMINISTRATION

NATHANIEL W. FAXON, M.D.

I—THE COCOANUT GROVE DISASTER

THE COCOANUT GROVE was a typical night club. It was a one story stucco and brick building, with low ceilings and inflammable hangings and decorations. On the evening of November 28, 1942, it was filled with an unusually large Saturday night crowd. The reported capacity was 600; the estimated number present was 1000. The several bars were crowded, the tables were filled to capacity, with every available bit of floor space occupied. The floor show was about to begin.

Fire started in the Melody Lounge, a basement cocktail lounge, about 10:15 P.M. Feeding on combustible decorations, artificial cocoanut palms and cloth-covered ceilings and walls, it spread with great rapidity to the stairs, cutting off the only visible means of exit. Then it flashed across the ceiling of the main floor. People rushed for the main doorway, the only exit that they knew of, where a revolving door quickly jammed, and some 200 victims were piled behind it. The flames then spread to the Broadway Cocktail Lounge where 100 more victims were trapped behind a door swinging the wrong way, which blocked access to the outside doorway. A door leading from the main floor was partially opened by an employee, through which a few escaped. Other exits were hidden by hangings and also locked. All agree that the spread of flame was rapid, with much smoke and noxious gases, and the lights went out quickly.

The fire department responded promptly and in adequate force. They opened doors, broke in windows, extinguished the fire, and rescued as promptly as possible all who were still alive, but 491 people lost their lives, either there or later in hospitals. Many others were seriously injured. One hundred and eighty-one living victims were taken to hospitals together with nearly 300 who were dead on arrival. Thirty-nine living patients arrived at the Massachusetts General Hospital, 131 at the Boston City Hospital, and the 11 others at various nearby hospitals. During the next two weeks, 39 patients died in hospitals—seven at the Massachusetts General Hospital, and 32 at the Boston City Hospital.

II—A BRIEF ACCOUNT OF THE SERVICES OF THE MASSACHUSETTS GENERAL HOSPITAL IN CONNECTION WITH THE COCOANUT GROVE DISASTER

The Cocoanut Grove fire started about 10:15 P.M., Saturday, November 28, 1942. The first patients arrived at the Emergency Ward of the Hospital at 10:30 P.M. Shortly thereafter the hospital was notified of the disaster and asked to be ready for a large number of patients. The hospital organization set up under "Civilian Defense" for the handling of war casualties was immediately put into operation; the House Staff and nurses on duty were

called to the Emergency Ward; Teams for Burns and Resuscitation were summoned; members of the visiting staff, nurses off duty, social workers, volunteers, orderlies, and others were notified. By 11:15 P.M. nearly the entire organization had been assembled, and volunteers continued to arrive during the night.

The Emergency Ward was immediately cleared of all other patients, but it was soon realized that its facilities would be overtaxed, and the sixth floor of the White Building, containing 40 beds, was evacuated. Thirty surgical patients were removed to other beds in the hospital.

Between 10:30 P.M. and 12:45 A.M., 114 casualties were received. Of these, 75 were either dead on arrival, or died within the first few minutes of uncontrollable anoxia.

The 39 living patients showed, besides burns of varying degrees, the effects of cold, exposure, fright, shock, and partial asphyxia. Clothing was dripping wet, exposed surfaces grimy and blackened. Some were quiet and cooperative. A few were comatose, others were greatly agitated, requiring restraint. In some this was due to hysteria; in others to cerebral anoxia (lack of oxygen supply to the brain). There was little or no evidence of intoxication. There were no fractures and only slight trauma of soft parts.

Wet clothing was immediately removed; burned surfaces covered with sterile towels and the patients wrapped in blankets. Morphine was given subcutaneously to all.

Meanwhile, four members of the House Staff had been stationed at the entrance of the hospital to determine whether those admitted were living or dead. Those pronounced dead were carried directly to an emergency morgue established in the large Brick Corridor; the bodies covered with sheets and the area screened off.

Some of the dead showed no burns; others showed burns of varying degrees, but death evidently had come from asphyxia in most cases. Many showed the cherry-red color indicative of carbon monoxide asphyxia. A few were severely burned; one almost beyond recognition. Identification of the dead was started at once, and all but two of the men were identified by 5:00 A.M. Identification of the women was very difficult on account of the lack of identifying data in their clothing. They were identified only by direct inspection by relatives or friends.

Preliminary treatment having been given to the living in the Emergency Ward, they were moved to White-6. By 1:30 A.M. all the living, 39 in number, had been put to bed in this ward. Burns had been dressed, shock was being treated, and asphyxia cases given oxygen therapy. The Emergency Ward was cleared and ready for more admissions. Thirty of the 39 patients had surface burns of clinical significance and many showed evidence of damage to the respiratory tract. In some this was very severe. In some cases it developed 24 hours later. In one case artificial respiration was required for the first six hours. The patient recovered. Five cases required tracheotomy and in one or two tracheal intubation was performed.

HOSPITAL ADMINISTRATION

The surface burns were treated by a single method. There was no cleansing or débridement. The burned surfaces were covered with gauze impregnated with boric petrolatum and a voluminous dressing applied with elastic pressure bandages. Splints of folded newspaper were used for forearms and hands. Eyes were examined by Staff and Residents from the Massachusetts Eye and Ear Infirmary and appropriate treatment instituted in the cases with lesions involving the cornea.

Blood plasma from the hospital blood bank was administered to 29 patients. By 1:00 A.M. all patients in impending shock were receiving plasma. Salt solution and glucose solution had been previously administered intravenously and was continued thereafter for long periods in many cases. In the first 24 hours 120 units of frozen plasma were used; in three days a total of 147 units. In addition, 16 whole blood transfusions were given in the first week, where there was reduced oxygen capacity. Teams of interns and nurses under the direction of surgeons, residents and the chief anesthesiologist were assigned to individual patients and to groups, and were in constant attendance. There were 20 trained nurses on eight-hour duty on this ward, or 60 each 24 hours. Oxygen therapy, directly by catheter or in tents, was given in appropriate cases, carbon dioxide five to seven per cent in oxygen was given to three patients, showing evidence of carbon monoxide poisoning. Sterile suction tubes for intratracheal intubation were used in several cases. In addition to the more intricate treatment routine intravenous medication, blood pressure determinations, blood tests, *etc.*, were carried out. Sulfadiazine had been given intravenously by 2:00 A.M. Sunday to all patients, including those without burns, and its administration was continued thereafter in appropriate amounts. All patients having been previously serum tested were given antitetanic serum, except Army and Navy personnel and those with serious pulmonary lesions.

By 3:00 A.M. Sunday a list of all the living, with names and addresses, had been made and given to police and press. During the first three days seven patients died. These were all cases showing severe respiratory tract damage from inhalation of flame or fumes. No cases of true bacterial pneumonia developed.

All the patients were segregated and isolated on the sixth floor of the White Building. Admission to the ward was strictly limited, with a doorkeeper in constant attendance. Besides professional staff and attendants only immediate relatives, clergy, family doctors, and officials on errands of importance were admitted, and all were masked and gowned.

The East solarium was converted into a dressing station where all dressings were done under the full aseptic precautions used in an operating room. Roentgenologic examinations of the chest were carried on in the South solarium on the same floor; all patients were so examined by 10:30 A.M. on Sunday, and thereafter as indicated.

The clinical laboratories were manned immediately on the night of the disaster and were kept busy continually thereafter. Hematocrit and serum protein determinations, to guide the administration of fluids and plasma, were

available that night, five times in all in the first 24 hours. Determinations of oxygen and carbon dioxide content of blood, oxygen capacity, nonprotein nitrogen, prothrombin time, blood chloride, phosphorus, sodium, and other tests, including various bacteriologic examinations, were also made.

The pathologic laboratory was called into action in making tissue examinations and later in performing autopsies.

Invaluable service was rendered by members of the Social Service Department. They helped in various places where needed. Their training and skill in dealing with people emotionally disturbed fitted them for the trying tasks of interviewing distracted relatives and friends of patients, and in answering innumerable telephone calls. They also helped in the identification of the living and the dead.

The services of volunteers from the Ladies' Visiting Committee and the War Service Committee proved of great value. They were persons of poise and they knew the hospital.

Medical students assigned to the hospital, together with a group of Harvard undergraduates who had been doing volunteer work as orderlies for six months, some of whom were on duty, and others who came in afterwards, rendered valiant aid that night and thereafter. They also knew the hospital.

The Red Cross functioned smoothly in the emergency. The motor corps brought casualties to the hospital. The Nurses' Aides were of immediate assistance that night, and the next day large numbers replaced and relieved regular nurses on duty in other parts of the hospital. The Red Cross Canteen, in connection with the hospital dietary department, served coffee and sandwiches during that night, which was a great help in sustaining energy and morale of workers and giving comfort to relatives and friends.

Many private nurses from Baker Memorial and Phillips House contributed their services during spare time.

The Massachusetts Women's Defense Corps sent volunteers who aided in identification and also were of great help with the Blood Bank.

Over 100 outside nurses from neighboring institutions volunteered and were put to work.

The regular staff of the hospital, administrative, medical, surgical, and special, nurses, orderlies, technicians, telephone operators, secretaries, dietitians, porters, maids, and maintenance personnel labored long hours at night and Sunday without stint.

In conclusion, it may be said that the hospital organization met the emergency adequately and well. Much credit should be accorded to the Civilian Defense organization for having made the hospital "catastrophe minded" beforehand. There was no shortage of supplies or equipment of any kind.

III—WE LEARN FROM OUR MISTAKES AS WELL AS FROM OUR SUCCESSES.
WHAT HAS THE MASSACHUSETTS GENERAL HOSPITAL LEARNED FROM THE
COCOANUT GROVE DISASTER?

1. First of all, we have learned the value of anticipation and preparation.

HOSPITAL ADMINISTRATION

Thanks to the efforts of the Massachusetts Committee for Public Safety or Civilian Defense we had been made "catastrophe minded." Our Staff and personnel had been organized as teams, their duties carefully specified, information regarding disaster management spread widely, and practice mobilizations carried out. Although during the first two hours everything seemed to be in confusion because of the numbers of people hurrying about, it was clear to those responsible that everyone was acting rapidly, efficiently and intelligently. They knew what they should do and were doing it.

Furthermore, we learned the value of having on hand what might have been considered an unnecessarily large quantity of supplies. Fortunately, no shortage of anything was experienced.

2. The value of a well-planned telephone service to notify administration, staff, nurses, technicians, maintenance and department heads should be especially emphasized. Too much thought and planning cannot be given to this service.

3. The necessity of the immediate examination and separation of the living and dead at the very entrance of the hospital. This was only realized after a number of dead had been sent to the Emergency Ward. At once, four Medical house officers, in teams of two, were stationed at the Emergency Ward entrance for this purpose. It is important that two men should collaborate.

4. The organizing of teams of nurses and assistants for the undressing of patients, of the affixing of identifying tags, and for the care and marking of their clothing and belongings. Those entrusted with the medical or surgical treatment of patients have no time for this, and the identification of patients separated from their clothing may be difficult. Likewise, clothing and valuables may get hopelessly mixed.

5. Special medical teams for the administration of morphine, the treatment of shock by plasma and oxygen therapy, were found to be valuable.

6. Prompt examination of the dead by competent pathologists, Medical Examiner or hospital pathologists, may provide clinicians with valuable data which will aid in treatment of the living. Autopsies upon those dying after clinical appraisal of symptoms are particularly helpful. The findings provided by autopsies performed and authorized by the Medical Examiners of Boston were of great assistance.

7. Handling of the dead: From our experience we learned that an Emergency Morgue should be selected in advance, paying attention to accessibility, isolation, windows for ventilation and cooling. It should be at once placed in charge of some responsible person and a police guard obtained as soon as possible. Only persons bearing passes acceptable to the person in charge and to the police should thereafter be admitted. The bodies should be arranged in orderly fashion, heads in the same direction, sexes separated if possible and covered with sheets. Tags numbered consecutively (M. G. H. 1, 2, 3, etc.) bearing date and hour of arrival should be attached to the right wrist. The Medical Examiner or Coroner should

be consulted as soon as possible and his directions followed. If he so directs, identification of the dead may be carried out. The name of the dead person can then be added to the tag. Also, at that time, valuables, pocketbook and cards may be placed in an envelope bearing the same number as the tag and attached to the left wrist. No jewelry should be removed.

However, if the Medical Examiner so directs, a complete list of all valuables can be made by two persons, one preferably a police officer; the valuables placed in an envelope, signed by the two persons and placed in a safe.

8. A list of living casualties and a list of identified dead should be prepared as quickly as possible and sent to the Information Desk. There it should be arranged alphabetically; several typed sheets prepared, and the information given to the police and press. All inquiries should be directed to this Central Information Desk.

9. In a disaster of this type, where the injuries were all of the same kind, the importance of concentration of casualties in one group in one ward or floor where they can be under concentrated medical treatment and where isolation procedures may be set up if needed, was clearly demonstrated.

In this disaster, a problem was presented by the abrupt and unexpected confinement in the hospital of 39 seriously injured people of private patient status. Isolation precautions were considered imperative and this had to be explained to anxious families. Many requests were received for transfer to private rooms for private medical care at the hospital or other institutions. The policy was immediately announced that visits from family doctors or consultants at the request of patient or family would be welcomed. The local medical profession cooperated whole-heartedly. Doctors visited their patients, reassured them and advised them under no condition to consider removal. Medical information which had a bearing on their present condition was often given to the Staff.

It is the mature judgment of those who cared for these patients that this concentration and this isolation prevented, to a large degree, respiratory complications and permitted better treatment. Doctors, nurses, equipment and supplies were concentrated here, quickly available for emergency treatment. Time and labor were saved.

10. It is desirable to obtain speedily police assistance to control yard traffic and to guard hospital corridors and morgue.

11. The serving of coffee and sandwiches by the Dietary Department and the Red Cross Canteen was valuable in sustaining energy and morale of workers and comforting waiting relatives and friends.

12. Finally, we have learned the value of constantly maintaining, for use in peace or war, a hospital organization for the handling of emergency disaster; also the collection of an ample quantity of emergency supplies.

"An emergency anticipated and prepared for ceases to be an emergency."

SOCIAL SERVICE ACTIVITIES

IDA M. CANNON, L. H. D.

FROM THE SOCIAL SERVICE DEPARTMENT OF THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON

THE CASUALTY PREPAREDNESS PROGRAM at the Massachusetts General Hospital delegated to the Social Service Department several areas of responsibility in keeping with their recognized function. These were:

- I Identification and registration of victims, in assistance to Hospital Admitting Officers. Reporting list of victims to Master File conducted by the Committee on Public Safety.
- II Arranging for transfer of such patients as were suitable for discharge to their own homes, convalescent or nursing homes or other hospitals, to relieve the wards for admission of victims.
- III Maintenance of Information and Advice Service to families and friends of victims. This to relieve the Hospital Information Service.
- IV Liaison with Red Cross Disaster Relief in their service to victims and with Public Safety District Information and Advice Bureaus.

Members of the Department had shared in practice with other hospital personnel in accordance with the Manual of the Casualty Preparedness Program for war-caused disaster. Although the "pattern" of the Cocoanut Grove disaster differed from the type anticipated in practice, the essential characteristics of social service activities were realized.

Social Service staff was not called promptly, but by 12:30 A.M. Sunday, four members of the Social Service staff were at the hospital and during Sunday 20 workers were involved. Twenty-four-hour service was maintained for the first two days, and 12-hour service for the first week.

Prompt shifting of patients from the especially chosen ward to other parts of the hospital had obviated the necessity for discharge of patients to make room for a flood of admissions. The urgency of admission of victims to the prepared special ward and the need for immediate treatment necessitated completion of identification *en route* impossible, and a social worker assisted in listing the victims and arranged an alphabetical list for use of the Admitting Office and for report to the Master File. As there were two unconscious unidentified women on the ward, she attended one of the doctors as one of the patients was aroused sufficiently to give her name. The other was correctly identified by a patient nearby. By 3 A.M. all 39 living victims were immediately pressed into service by the nurse at the hospital Information Desk. Two, and at times three social workers assisted here throughout the night and morning. Three telephones brought incessant

inquiries. Being at the hospital entrance, it was here that a restless throng soon assembled. Members of the press and police eager for lists of victims, representatives of army and navy seeking identification of their men, blood donors in great numbers responding to the urgent radio appeal. One zealous young man brought in several groups of prospective donors he had enticed from passing street cars. These people, at first directed to the Blood Bank Station, were later sifted by a responsible volunteer by questions of time of latest food and liquor intake.

To get some idea of the pressure at the Information Desk, one must realize that while the doctors and nurses were absorbed in giving care to the living victims, and the Administration was wrestling with the problem of an improvised mortuary for the 75 dead, the community was being aroused to the magnitude of the tragedy by radio and swift traveling news. Families and friends were setting out anxiously to locate some 650 missing persons.

The listing and reporting of the 75 dead in the improvised mortuary were delayed partially awaiting authority from the Medical Examiner, and also because of the serious difficulty in identification. The process of identification was shared by the police, Women's Defense Corps and various hospital personnel. Most of the men had identification in their pockets. These were listed and reported. But the women, who were mostly in evening dress, were without handbags or coats. Their clothing was often torn and burned. Jewelry proved to be an important means of identification.

In increasing numbers through the early morning and into Sunday afternoon the anxious relatives and friends came, some from considerable distance, singly, but more often in groups. For some their visit here was the first effort to find the missing victim. Some of them had already checked with the Master File and knew that there was no evidence that the one they sought was among the living. Some had already made the rounds of the mortuaries. The major task of the Social Service Department at the hospital entrance was meeting and interviewing these relatives and friends of those seeking victims. Some 175 interviews were recorded. In spite of extreme tension, shock and physical weariness these men and women acted with great dignity and restraint. There was no hysteria. In comment on the technic for handling the situation, we note that the inquirers awaiting interview were restless and needed to move about. Many wanted to smoke and were not denied. They were interviewed in turn by the Social Service Staff. For the interview which served as some release of tension, they were seated and in a separate room, which gave some privacy. The interview in introduction followed something of a pattern: The name of the victim sought, relation to inquirer, a review of list of living. Although in some instances this was a repetition of review at the Information Desk, another search for the familiar name was anxiously sought. Hope lingered. Then after explanation that there were unidentified dead, we proceeded to get age, height, weight of victim, whether blonde or brunette, description of

SOCIAL SERVICE ACTIVITIES

clothing, and especially jewelry. Meantime some descriptions of women victims with special note of jewelry had been assembled with the hope that these descriptions might be checked with inquirers' descriptions and so avoid the painful necessity of having the relative view several victims in the process of identification. This proved helpful in a few cases. More accurate description of victims and better system might have made this more helpful. So far as possible, visitors were accompanied by volunteers or Social Service on their visit to the improvised mortuary. Medical Social Service assisted at the mortuary where all inquirers were required to register. If identification was established, the relative was accompanied to the Admitting Office. If not, the next step was suggested. The address and telephone number of the Master File and other hospitals were given. By 5 P.M. Sunday, identity of all but two men had been established.

At the request of the Admitting Officer one worker was assigned to telephone to some 60 patients who had appointments for admission during the ensuing week, explaining the necessity for postponement on account of the admission of disaster victims. Another worker was asked to call families of those dead whose homes were at a distance and explain the situation.

Our experience has convinced us that during a disaster no services can be considered mechanical. Giving information or compiling data and making records require a degree of judgment and skill not demanded under ordinary circumstances. Because of the extreme emotional tension under which people are suffering and the stunned sense of isolated bewilderment, instructions are often not readily comprehended. Customary routine, such as asking for information, needs to be individualized and far more skill in interviewing is required. Even the briefest contacts become charged with meaning and often the simplest services are valuable out of all proportion, such as dialing a telephone number for a confused relative.

On Sunday, the morning following the disaster, at the request of the Supervisor acting as head nurse in the special ward, two medical social workers were assigned to the ward, one to attend the telephone line over which inquiries about patients were routed, the other to control admissions to the nurse's desk to answer telephone inquiries about patients rapidly developed into a fuller service. In cooperation with the head nurse an up-to-the-minute report on condition of the patients was maintained so that reports could be readily given to relatives. The patients, at first too stunned to realize the situation soon began to ask questions. What had happened to wife or husband? Where were the others in the party? Had they escaped? Many patients had members of family and friends who were also victims. The living and dead members of groups were widely scattered. Messages of inquiry and reassurance passed rapidly to-and-fro. The information ac-

cumulated was useful to the doctor in dealing with problems of when and how to inform the patient about the death or condition of other members of the family or party.

On direction of the Administrator on duty, incoming mail to patients was opened, read, and wherever there was question about reading certain messages to a patient, the approval of the doctor was secured. Many patients had bandages over their faces which prevented use of their eyes, and so it was important to read mail to them. Messages, letters and telegrams from patients were handled by Social Service for them.

Practical problems distressed patients and needed attention. Among these were witnessing a will, attending to insurance papers, inquiries about clothing and valuables, transfer of automobiles left near the scene of the disaster, job adjustments and communication with employers, letters to be written, household arrangements such as messages to maids at home, care of pets, liaison with army and navy authorities. Discrimination was necessary as to what could be handled by the social worker and what needed clinical or administrative sanction. There was need for some exercise of judgment and counseling also in relation to the patients' or families' requests which under the stress of the situation sometimes showed hasty ill-advised decisions.

On the third day, at the request of the staff doctors, the social worker on duty accompanied the doctor as he interviewed relatives who were still excluded from the ward. This interview served to establish in the visitors' minds the fact that the social worker was working with the doctor and that she could be used for interchange of messages and interpreting the patient's condition. A special attempt was made to relieve the emotional stress of the relatives by giving them an opportunity to talk. Some of them had special need for this. For instance, the father summoned from a distant city because of the imminent death of his daughter but arriving too late to clear up a misunderstanding between the daughter and her mother.

By previous agreement one of the Social Service Staff had been appointed liaison with the Red Cross Disaster Relief. Their resources had been promptly offered. Although most of our patients were in comfortable economic circumstances there were some serious and urgent needs for advice and guidance in meeting the necessary adjustments, especially for families at a distance. Daily intercommunication with the Red Cross was established early. Their generous outpouring of helpfulness, material and friendly, is another story.

Under the urgency of a disaster such as this the focus of clinical concern of the physician and nurse is sharpened, the area of attention markedly restricted. At the same time the personal and social aspects of the patients' problems are especially acute and distressing. For them the experience of sudden shift from well-being and gaiety to painful and serious injury, and for many the death of some loved ones, created deeply disturbing complica-

SOCIAL SERVICE ACTIVITIES

tions that needed special psychiatric attention. Deep grief experience came to many patients at a time when they were enduring physical suffering and, immobilized and isolated, they could not act for themselves. The necessary "no visitors" precaution made it more difficult to turn to their families for help.

Only by well-integrated teamwork among all the professional personnel charged with the responsibility for service to patients could the total situation of each patient become comprehensible and be dealt with. This teamwork at the time of the disaster can be sustained and function only on a foundation of previous teamwork experience and mutual confidence. Thus Social Service was prepared to carry its own responsibilities and also some of the personal service to patients carried by nurses and doctors in the usual day's work. We are well aware that after all the various professional skills are expended in meeting the patients' acute needs, there are left for many of them broken homes, responsibility for care of fatherless children and loneliness, wounds which time and inner resources alone can heal.

NEUROPSYCHIATRIC OBSERVATIONS.

STANLEY COBB, M.D., AND ERICH LINDEMANN, M.D.

FROM THE DEPARTMENTS OF PSYCHIATRY, MASSACHUSETTS GENERAL HOSPITAL, AND OF NEUROPATHOLOGY
HARVARD MEDICAL SCHOOL, BOSTON, MASS.

THE STUDIES to be reported here do not deal with all the neuropsychiatric abnormalities which occurred on the Disaster Ward. Mild transient confusions and delirious conditions, fluctuations in consciousness, fleeting periods of restlessness were handled by surgeons and medical men without the need for a special psychiatric inquiry.

This report deals rather with the problems involved in the emotional adjustment of the patient to the disaster, with all its implications—disfigurement, lasting disability, loss of work, bereavement, and disturbed social situations. We wanted to learn how to recognize those patients who are liable to emotional disorders, to prevent such disorders if possible, and to help those who had become victims of untoward emotional reactions.

The first request for psychiatric help came through the social workers who were serving as liaison personnel with relatives and friends. They soon had become aware of the fact that the emotional upset which followed the discovery of a body had attained, in some of the relatives, the proportions of a major psychiatric condition and needed trained intervention, and it was at their insistence that we first witnessed the states of acute grief which will be discussed in detail later in this study.

From observing violent reactions in the relatives, we concluded that similar reactions might occur in the patients on the ward as soon as they were recovered enough to deal with the disruption of their social relationships.

The social workers continued to confer with the psychiatrist about the management of milder reactions and were extremely helpful in the arrangement of the subsequent systematic studies.

On the eighth day after the disaster, the psychiatrists were invited to review all patients still on the ward. The occasion was a dramatic psychotic episode in a woman who had not been confused and was not then showing signs of impairment of brain functions, but who had responded to the news of the death of her husband and son with a state of excitement and intense paranoid suspicions about the ward personnel. She also believed that nurses and doctors were considering her an immoral, sinful person and were plotting to detain her and to prepare for her punishment. She insisted upon leaving against the advice of the physicians and was able to persuade members of her family to demand her release. Psychiatric inquiry showed that this patient had had a former episode of mental abnormality with obsessive fears, depression, and mild agitation. Follow-up reports show that her subsequent adjustment has remained quite precarious, with spurts of over-activity alternating with periods of apathy but that she has not developed any frank psychosis.

NEUROPSYCHIATRIC OBSERVATIONS

In the light of this incident it was decided to make a brief psychiatric study of all the patients left on the ward in order to be able to anticipate subsequent emotional disturbances. Seventeen patients have been so reviewed. Each received a neurologic and psychiatric examination. Abnormalities in mental status were recorded. A psychiatric history was obtained from the patient, and with the help of social workers from the relatives. Plans were made with surgeons, social workers, and the occupational therapy workers for the best care of each patient in the light of our observations about his emotional reaction patterns and his former modes of adjustment. The group as a whole was of fair intellectual level. Except in one case there was no aphasia or apraxia, and the disturbances of memory were limited to amnesic scotomata, which was difficult to separate from the effects of impairment of consciousness at the time of the accident. The one case that showed neurologic symptoms with signs of cerebral lesions is described first:

One patient showed a clear-cut picture of cerebral lesion. This was a married woman, age 35, who was admitted in profound shock, with stertorous breathing. She was quite red, and carbon monoxide poisoning was diagnosed. At 11:30 P.M. oxygen was started and she had become active and noisy, but was out of touch with her surroundings. Twelve hours later she was still restless and disoriented; she occasionally spoke short sentences that had little relation to the situation. By 7:00 P.M. she was extremely restless, thrashing about with her arms and legs and had to have restraint and sedation. After that she was quiet for 12 hours. During the next three days she alternated between periods of motor activity and periods of quiet due to sedatives. When aroused she thrashed about. On December 3, it was noted that the movements were definitely athetoid and were accompanied by facial grimaces. These movements reached an apex on the fifth to tenth days, when she showed a full-blown picture of athetoid chorea, especially marked on the left side. Along with this there was jaundice, semicomatose and speechlessness.

The picture of athetoid chorea was gone by the fourteenth day. During the next two weeks the patient began speaking but showed marked aphasia, which resolved into a dysarthria plus extensive memory defect (31st day). The memory improved over the next six weeks, so that she could remember events for a number of hours and even up to three days. It is very much impaired even at the last examination (94th day); she remembers facts that she did certain things, such as that she had lunch with a certain person, she seems to have lost all ability to revisualize, to remember what the scenes were like, and how people looked and even how objects looked. The dysarthria remains.

Diagnosis.—There was evidently an extensive asphyxia of nerve cells of the brain. This appears to have been very widespread and to have affected both the basal ganglia and the cortex. In the cortex there is no special localization except that the lower end of the motor area in the left hemi-

sphere seems to have been especially affected and the temporal lobe seems to have been largely spared. The worst lesions are probably in cortical areas 19, 39, 9, 10 and 11, on both sides, with the lower part of areas 4 and 6 on the left. The right striatum is probably degenerated more than the left, but most of the damage to the basal ganglia seems to have been acute and reversible.

PSYCHOTIC CONDITIONS PRIMARILY PSYCHOGENIC

Two patients developed frank psychotic episodes and in both instances the former history showed clear-cut indication of previous maladjustment:

A young man had received only minor burns and left the hospital apparently well on the road to recovery just before the psychiatric survey took place. On the fifth day he had learned that his wife had died. He seemed somewhat relieved of his worry about her fate and impressed the surgeon as being unusually well-controlled during the following short period of his stay in the hospital. There seemed to be no occasion for any psychiatric attention.

On January 1 he was returned to the hospital by his family. Shortly after his return home he had become restless, did not want to stay home, had taken a trip to relatives trying to find rest, had not succeeded, and had returned home in a state of marked agitation, appearing preoccupied, frightened, and unable to concentrate on any organized activity. The mental status presented a somewhat unusual picture. He was restless, could not sit still or participate in any activity in the ward. He would try to read, but drop it after a few minutes, try to play ping-pong, only to give it up after a short time. He would try to start conversations, break them off abruptly, and then fall into repeated murmured utterances: "Nobody can help me. When is it going to happen? I am doomed, am I not?" With great effort it was possible to establish enough rapport to carry on conversations. He complained about his feeling of extreme tension, inability to breathe, generalized weakness and exhaustion, and his frantic fear that some terrible thing was going to happen. "I'm destined to live in insanity or I must die. I know that is God's will. I have this awful feeling of guilt." With intense morbid guilt feelings, he reviewed incessantly the events of the fire. His wife had stayed behind. When he tried to pull her out, he had fainted and was shoved out by the crowd. She was burned while he was saved. "I should have saved her or I should have died, too." He complained about being filled with an incredible violence and did not know what to do about it. The rapport established with him lasted for only brief periods of time. He then would fall back into his state of intense agitation and muttering. He slept poorly, even with large sedation. In the course of four days he became somewhat more composed, had longer periods of contact with the psychiatrist, and seemed to feel that he was being understood and might be able to cope with his morbid feelings of guilt and violent impulses. On the sixth day of his hospital stay, however, after skillfully distracting the attention of his special nurse, he jumped through a closed window to a violent death.

NEUROPSYCHIATRIC OBSERVATIONS

A young unmarried woman with severe burns of face, back, hands, and feet, more restless than the other patients during the first week, developed a strong attachment to her special nurse, resisted the care given by others, but remained fairly inconspicuous until January 2, when she developed a state of excitement with violent aggressive behavior, vulgar language, and furious refusal to cooperate with the nurses. She slept poorly, refused food, and disturbed the rest of the ward with her noisy behavior. She became a serious problem in nursing care. She had a period of four weeks of fluctuations in mood, apathetic, tearful periods alternating with outbursts of aggression, and in the first week of February again was excited, refused food, and became incoherent, hallucinated, and preoccupied with fantasies of destruction and violence.

The past histories of both these patients were obtained in detail, and showed evidence of inadequacy, with a tendency to retire from social contacts and to develop psychotic manifestations in situations of stress.

PSYCHONEUROSES

A history of a frank neurosis in the past was present in two patients. They did not show any signs of mental derangement during the hospital stay and did not become serious nursing problems. Their difficulties became most conspicuous after discharge from the hospital. The return to normal life activities was slow and previous psychoneurotic manifestations recurred in exaggerated form, requiring systematic psychiatric therapy.

One woman had severe burns of face and hands and was threatened with marked disfigurement during the first period of her stay. She was extremely worried about her appearance and needed frequent reassurance. Her recollections of the disaster are that she was walking upstairs. By the time she got up there she already found herself stumbling over many bodies and was afraid that she would not reach the door. She felt suddenly that the fire was God's punishment because she had fallen below her standards. She prayed aloud and other people fell in with her prayer. While she was praying she somehow was shoved over piles of dead bodies and finally her hand reached out "into fresh air." The whole picture is now extremely clear to her and returns to her mind at frequent intervals.

Her course in the hospital was fairly smooth. The only symptom was her intense fear of being left alone in the interview room she followed since discharge. She finds it impossible to attend any gathering place. Visiting a restaurant with her family, she had a vision of fire breaking out, of tables and chairs being tipped over, and left the room in frantic fear without having eaten anything. She had a similar experience of return of memories of the fire when she tried to attend a movie.

Another young woman has had frequent attacks of anxiety ever since

puberty. These consist of trembling, heart palpitation, choking sensations, and the fear of impending disaster. She had not obtained any adequate help for her psychoneurotic symptoms and restricted her social activities and occupational plans because of them. She had come to consider her life a failure. The Coconut Grove incident had seemed to her the final fulfillment of all her fears. During her convalescent period in the hospital she was a very cooperative, if somewhat discouraged patient. Except for her timidity and anxiety, she had no emotional difficulties during her hospital convalescence, but after she left the hospital she was unable to make a satisfactory home adjustment. She feels too disfigured, believes she has no chance for further happiness, and is hopeless about the future. She is being continued in regular psychotherapeutic interviews.

The other patients did not show any significant history of previous psychiatric difficulties. None of them had positive symptoms of neurosis, psychosis, or personality defect.

REACTIONS TO BEREAVEMENT

Seven patients became problems of psychiatric study and management because their recovery was complicated by severe grief. This study provided an unusual opportunity to observe the mechanisms of grief by which the bereaved person reestablished his equilibrium after the loss of a beloved.

Within a few days after the incident, as soon as the patient recovered from the shock and clouded consciousness, the question arose of when to tell him about his loss. It was obvious that both the physical and mental condition must be such that the individual could tolerate the message.

Our observations concern seven bereaved patients. Three of them said that they had been told just at the right time. Three felt that they had been reasonably certain of the loss and the final confirmation appeared as a relief of uncertainty rather than as an additional shock. One patient suspended all inquiry about the details of her husband's fate for more than four weeks, deliberately occupying her thoughts with personal friends and pleasant fantasies and recollections. When, however, her relatives visited her, they became more and more uneasy because the range of topics discussed in conversation was necessarily small. Any reference to the lost person and any attempt at planning the future had to be avoided. It finally became the psychiatrist's task to confront the patient with the sad news. This was done in the slow process of gradually recalling to her the details of her family life, her relationships to her children and relatives, and making it inescapable for her to inquire positively about the fate of her husband. Her first reaction was to blame her relatives for withholding the news and in the subsequent interviews there was a marked hostility against the psychiatrist. After a grief period of less than a week she continued to make an unperturbed recovery so far as her physical condition was concerned. She has refused any further relationship with the psychiatrist but has apparently made a fairly good adjustment at home.

NEUROPSYCHIATRIC OBSERVATIONS

Frequent discussions between the surgeon and the psychiatrist were necessary to weigh somatic and psychologic factors bearing on the right moment of delivering the message of bereavement.

The second task of the psychiatrist was to assist the person with the adjustment to the loss and to steer him through the disturbing period of intense emotional upheaval which ensued during the subsequent weeks. It became apparent that the different patients showed considerable variation in their reactions. Common to all of them, however, was the following syndrome: Sensations of somatic distress occurring in waves lasting from 20 minutes to one hour; a feeling of tightness in the throat, choking with shortness of breath, need for sighing, and an empty feeling in the abdomen, lack of power in the muscles, and an intense subjective distress described as tension, lonesomeness, or mental pain. The patient soon learned that these waves of discomfort could be precipitated by visits, by mentioning the deceased, and by receiving sympathy. There was a tendency to avoid the syndrome at any cost, to refuse visits lest they would precipitate the reaction, and to keep deliberately from one's thoughts all references to the deceased. Three men appeared in the psychiatric interviews to be in a state of tension, with tightened facial musculature, unable to relax for fear they might "break down." It required considerable persuasion to yield to the grief process before they were willing to accept the discomfort of bereavement. One of the patients assumed a hostile attitude toward the psychiatrist, refusing to allow any references to the deceased and rather rudely asking him to leave. This attitude remained throughout his stay on the ward, and the prognosis for his condition is not good in the light of other observations. Hostility of this sort was encountered on only occasional visits with the other patients. They became willing to accept the grief process and to embark on a process of dealing in memory with the deceased person. As soon as this became possible there seemed to be a rapid relief of tension and the subsequent interviews were rather animated conversations in which the deceased was idealized and in which misgivings about the future adjustment were worked through.

It seems that the grieving person can delay his grieving period but not avoid it, and that individuals who show no signs of grief during the period of convalescence from their somatic injuries are likely to have disabling disturbances at a later period. Prophylactic care is most important here. The patient must be allowed to carry through his grief reaction at the optimal time without undue delay; he must be assisted in his efforts to extricate himself from the bondage to the deceased, to be prepared to face the task of social readjustment when he leaves the hospital.

SPECIAL STUDIES

In addition to these problems of clinical management, the solution of certain research problems has been brought nearer realization through the cooperation of a group of patients. For some time, the Department of Psy-

GRAPHIC REPRESENTATIONS OF ACTION-SILENCE

Figures 1 to 7 present interaction chronograms which show the striking differences in activity rates observed in patients with acute grief and in those suffering from other forms of morbid depression.

Figures 2 and 3 represent mood disturbances which were seen in the Psychiatric Service. They showed depressive reactions with the usual slowness of response and underactivity. Figure 4 shows a patient who was found in a mild manic state of overactivity with euphoria and cheerful thought-content. Contrary to expectations, the interaction chronograms of bereaved patients, as shown in Figures 5, 6 and 7, show overactivity and no retardation and slowness of response as seen in other depressed states.

SCHEMATIC REPRESENTATION OF TAPE, FIGS. 1 TO 7 INCLUSIVE

To show actions, silences, double actions, and double silences (double actions and double silences reckoned from Subject A).

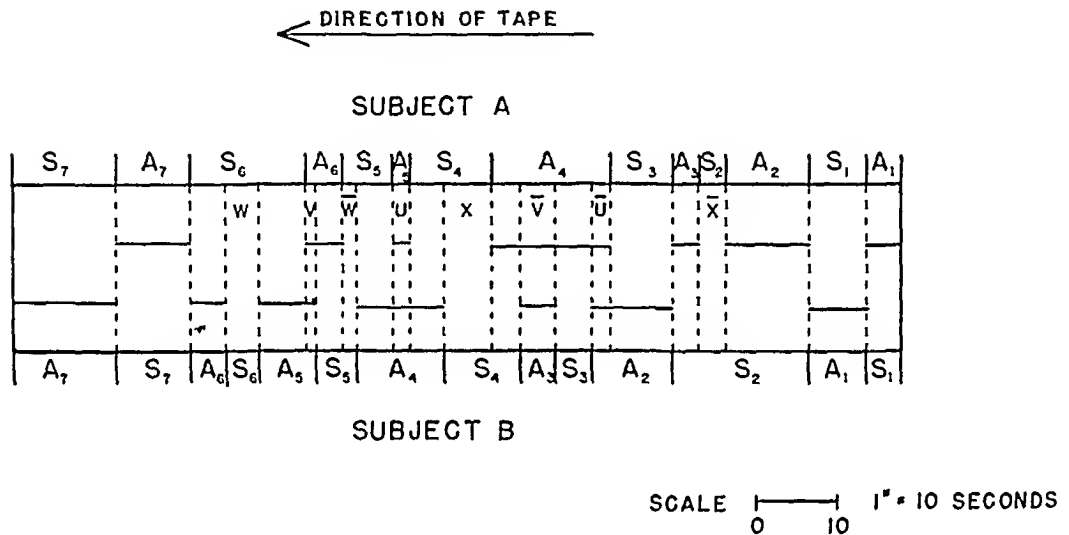


FIG. 1 shows the various symbols assigned to different events in interaction. (A)—activity (verbal or gestural), (S)—silence (inactivity), (u)—double action initiated by the patient (such as verbal interruption), (v)—double action initiated by the doctor, (w)—double silence due to failure to respond on part of the patient, (x)—double silence due to failure to respond on part of the doctor.

A bar over the u, v, w, or x (\bar{u}) indicates double actions or double silences after which the patient continues.

The tape moves at a speed of five inches per minute. An observer sits behind the screen and observes through a one-way window. She records on the moving tape by means of keys the activities of the two participants in the interview under the headings mentioned above. This tape is then mathematically analyzed to give the curves shown in Figures 2 to 7.

Figures 2, 3, 4, 5, 6 and 7 are graphic presentations in "cumulative series" of four types of relationships:

(1) A-S represents the relationship of the patient's periods of activity to his periods of silence. The more overactive he is the more positive is the slope of the A-S curve; the more underactive he is the more negative is the slope of this curve.

(2) u-w represents the relationship of the patient's double actions (such as his interruptions of the doctor) to his failure to respond.

(3) v-x represents the relationship of the doctor's double actions (such as his interruptions of the patient) to his failure to respond.

(4) θ -o represents the relationship of the patient's initiations of actions to those of the doctor.

CURVES IN ACUTE GRIEF AND RELATED CONDITIONS

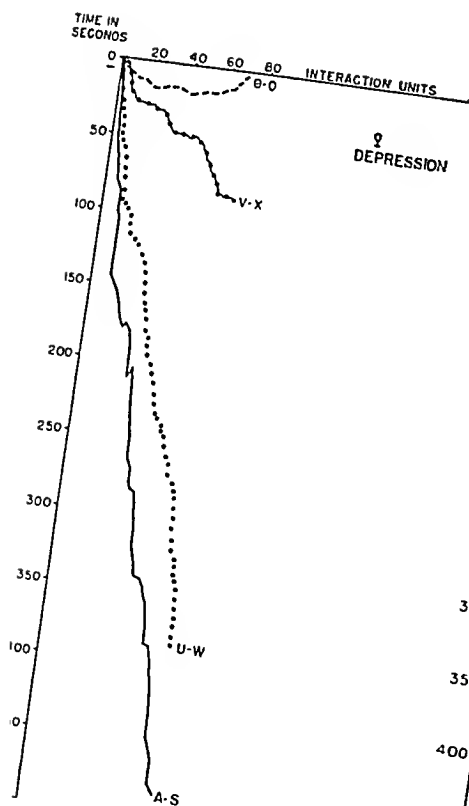


FIG. 2.—A morbid depression of mood not complicated by grief. Note the steep negative slope of the A-S curve and the U-W curve. The deficit of action in relationship to silence on the part of the patient is 480 seconds in a 40-minute interview.

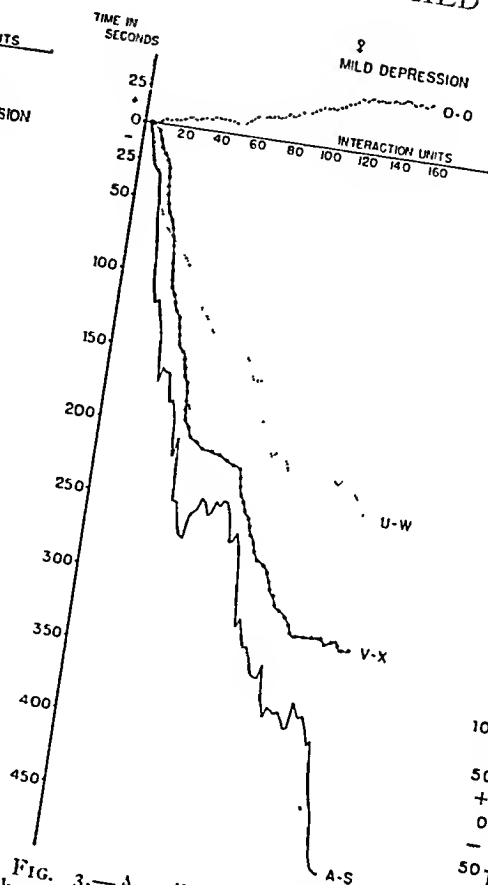


FIG. 3.—A milder depression. The steep negative slope of the A-S curve is interrupted by occasional periods of increased activity but there is still a marked deficit in action.

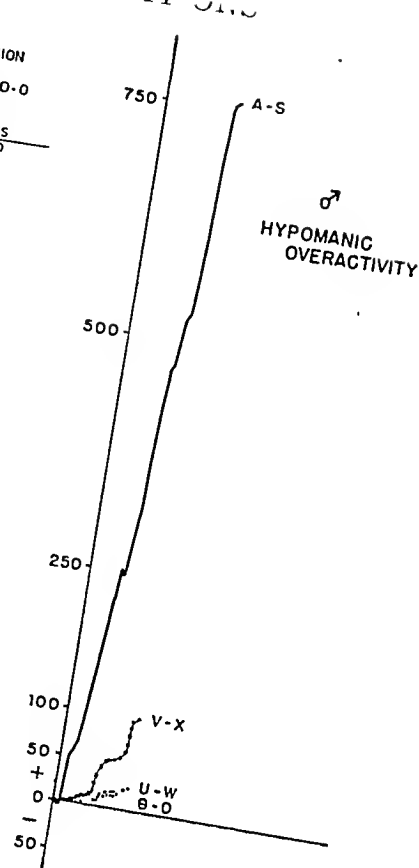


FIG. 4.—A patient in a mild manic episode with marked overactivity. The surplus of activity over silence in a 40-minute interview is 750 seconds.

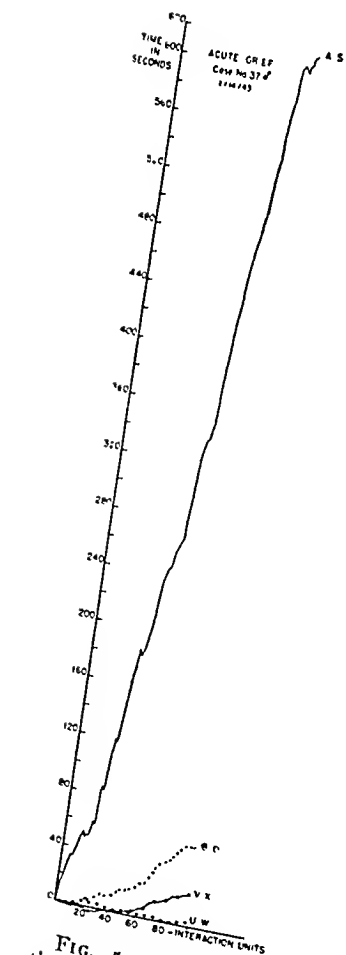


FIG. 5.—Acute grief reaction. The patient appears depressed during the interview but shows considerable overactivity. The A-S curve has a steep positive slope. The surplus of action over silence in a 40-minute interview is 610 seconds.

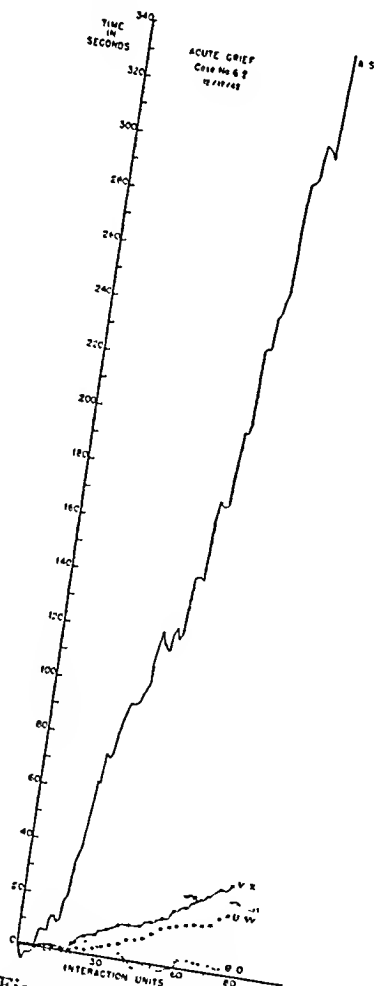


FIG. 6.—Acute grief reaction with strongly depressive thought content. Note the steep positive slope of the A-S curve. The curve resembles that of Figure 4. There is a marked surplus of activity over silence.

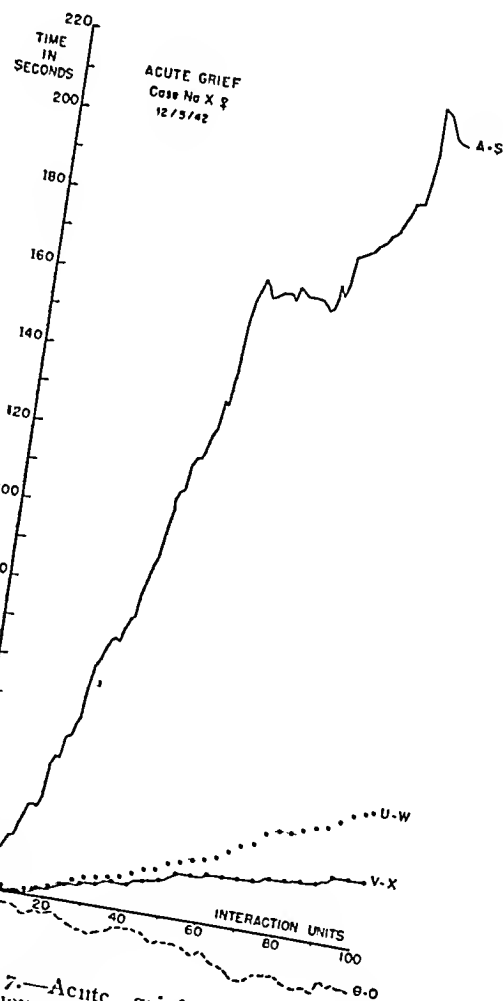


FIG. 7.—Acute grief reaction with less pronounced overactivity.

chiatry has been interested in the physiologic and psychologic aspects of acute grief. Since acute grief is one of the most frequent psychogenic factors found in patients with psychosomatic disorders, such as asthma, colitis, and rheumatoid arthritis, we have been anxious to discover what physiologic features of grief might play a rôle in contributing to the etiology of these disorders.

In the fire victims there was evidence of disturbances in autonomic functions. The pupils were generally large. During the surges of acute grief described above, there was usually sighing respiration, "hot waves" to the head, flushed face and perspiration. Systematic spiograms were not satisfactory because of the chest involvement. We have, however, been able to carry on observations in bereaved relatives who showed the same sighing respiration. The result of these studies will be reported elsewhere. There is indication that the altered respiratory activity, combined with the disturbance of sleep and appetite, may form the nucleus of a physiologic disturbance which forms the background for the "emotional distress" described by the patients.

Our data are somewhat more complete for the study of the amount of activity presented by the fire victims and bereaved patients. It is known that in states of morbid depression a patient is likely to be "retarded" in speech and action. Contrary to expectation, in the state of depression and unhappiness following such a disaster experience, there is not a reduction in activity as is seen in cases of psychotic depression; instead there is an increase in need for activity. This can be strikingly demonstrated by a new measuring device, the "interaction chronogram." The patients were examined during a psychiatric interview for the timing of their verbal and gestural activity. A record was made in this way of their interaction with the psychiatrist and a graphic presentation was furnished, showing the balance of activity and inactivity at any given time. These graphs furnish an objective record of the patient's capacity to be active, of his hesitations after questions, and of his tendency to "out-talk" the examiner in conversation. We found that all bereaved persons examined, showed a positive slope of the action-silence curve, indicating a surplus of activity over inactivity (Figs. 1-7). (For a brief description of procedure see Figure 1; for a complete description, ref. Chapple and Lindemann.¹)

This finding is of special significance because it indicates a drive for activity in individuals who at the same time complain about apathy, inability to initiate any action, and lack of interest in their ordinary pursuits. Our observations seem to indicate that there is a good deal of drive for activity and the lack of "conduct patterns" by which to express their drive. A good many daily activities were conditioned to the presence of the deceased and could no longer operate. But more than that, other activities not obviously connected with the presence of the deceased have lost their meaning and are carried out only with difficulty. It is, therefore, not surprising that only two of our series of mourning individuals were able to resume their ordinary

NEUROPSYCHIATRIC OBSERVATIONS

activities after leaving the hospital. The others still find themselves aimless, lacking in initiative, and looking to others for suggestions to follow. These observations are still going on, but already indicate the necessity of a careful follow-up study of both patients and relatives. We have made an effort to reach as many individuals involved in the tragedy as possible, but several months must elapse before any final conclusions can be drawn.

DISCUSSION.—Of 39 patients admitted to the hospital, seven died within 62 hours. Of the survivors, at least 14 presented neuropsychiatric problems. This high incidence may seem surprising, but it fits well with the experiences of psychiatrists working in general hospitals. Forty-five to 55 per cent of the patient population are likely to present psychologic factors in their problems.

Unless the psychiatrist has an opportunity to see all the victims of a disaster, danger signals and opportunities for help along psychologic lines may be overlooked, since they are by no means obvious to the untrained worker.

Conditions predominantly due to cerebral damage were rare, probably because they usually lead to death. Conditions predominantly due to psychogenic factors showed a high incidence. In all patients with clear-cut neuroses and psychoses, the psychiatric history offered clues as to the likelihood of such development under stress. This observation fits well with recent studies concerning traumatic neuroses in the armed forces.^{2,3} It seems well founded that induction boards refuse admission to the armed forces to candidates who show a former history of psychosis or psychoneurosis.

The more severe emotional disturbances encountered in formerly well-adjusted patients seemed to be due not so much to the impersonal effects of the disaster (fright and horror) as to the problems in personal and social relationships involving conflict and guilt. Similar observations are reported by Sargant,⁴ in 1940, and Wilson,⁵ in 1941, after the disaster experiences of members of the British armed forces and civilian population.

Psychiatric assistance in the solution of these personal problems and in readjustment after a social crisis forms an important part of the care of disaster victims.

SUGGESTIONS FOR FUTURE EMERGENCIES

Our observations seem to indicate that the psychiatrist can operate as a useful member of a disaster unit. His work may be divided into three phases: In the first few days severe shock and life-saving procedures occupy the field. Apathy and excitement, confusion and delirious states have to be handled by proper sedation and proper surroundings. In our present observations we have only indirect evidence of the victims' emotional states at that time. Two patients complained of the lack of a chance for enduring contact with one person—doctor, attendant, or nurse: everything seemed to change; every person who arrived seemed to be new; no information or outside news

was available; the days were ones of utter bewilderment, offering no frame of reference. It might be advisable to have the ward personnel as small as circumstances permit or so divided that patients have a chance to deal with the same person repeatedly.

The second phase deals with the psychiatric care of the convalescent patient, advising him in his transitory problems, determining when messages should be delivered or revelations made, and managing with the patient his efforts to readjust.

The third phase deals with the psychiatric care of the convalescent patient after he leaves the hospital and his proper readjustment in the community. We can, in this manner, have reasonable hope of preventing the occurrence of prolonged maladjustment or traumatic neurosis.

During the first phase, the psychiatrist's chief contribution is his aid to the relatives and his counsel to the medical social worker who is dealing with the numerous problems of family and work relationships. During the second, he is intimately involved with the internist and surgeon and must continue his contact with the social worker, which becomes even more important during the third, when social readjustment forms the center of interest. Throughout the whole of the three periods, not the least of the psychiatrist's responsibilities is determining what can safely be delegated to the medical social worker and guiding her in her efforts.

It seems fair to conclude that it is desirable to have psychiatric evaluation of patients early in the course of their hospital care, continued psychiatric attention to those patients who are in a precarious emotional state, and, lastly, aid in making readjustment, especially to bereavement, after leaving the hospital.

REFERENCES

- ¹ Chapple, E. D., and Lindemann, E.: Clinical Implications of Measurements of Interaction Rates in Psychiatric Interviews. *Applied Anthropology*, 1, 1-11, 1942.
- ² Ross, T. A.: *Lectures in War Neuroses*. Williams and Wilkins, Baltimore, 1941.
- ³ Gillespie, R. D.: *Psychological Effects of War on Citizen and Soldier*. Norton, New York, 1942.
- ⁴ Sargant, W., Slater, E.: Acute War Neuroses, *Lancet*, 2, 1, 1940.
- ⁵ Wilson, A. T. M.: Reactive Emotional Disorders. *Practitioner*, 146, 254-258, 1941.

RESUSCITATION AND SEDATION OF PATIENTS WITH BURNS WHICH INCLUDE THE AIRWAY

SOME PROBLEMS OF IMMEDIATE THERAPY

HENRY K. BEECHER, M.D.

FROM THE ANESTHESIA LABORATORY OF THE HARVARD MEDICAL SCHOOL, AND THE
ANESTHESIA SERVICE AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

CERTAIN ASPECTS of the Cocoanut Grove disaster are characteristic of conditions encountered in most conflagrations of the flash-burn type. In this report attention will be given primarily to the factors of general interest. These matters are particularly appropriate for consideration at this time, for in the present widespread use of mechanized warfare flash-burns are exceedingly common.

As the patients from the scene of the disaster were crowded into the hospital it became apparent early that they were divided sharply into two groups: The living and the dead or near dead. None in the former group died in the first 12 hours; none in the latter group lived more than a few minutes after arrival.

The patients who lay quietly at rest on arrival were in the minority. As soon as it could be established tentatively that these few individuals had not suffered central nervous system injuries or were not stupefied by smoke inhalation and showed no signs of approaching shock, it was clear that the larger, hyperactive group needed the most attention, although, at the same time, the importance of watching these quiet ones was not minimized.

An outstanding characteristic of the living group was hyperactivity, even to the extent of mania in some cases. One's first impulse is to assume that this hyperactivity is due to pain. From the history of other similar tragedies this appears to have been the usual assumption and the patients treated accordingly. A careful appraisal of the causes of this hyperactivity is of real assistance in planning individual therapy. In the Cocoanut Grove disaster we had a unique opportunity for simultaneous observation of a considerable number (39) of victims of the same accident. It was quite apparent that pain was an improbable cause of the observed hyperactivity in many cases. *As time progressed the importance of correctly diagnosing the cause of this hyperactivity in a given case became increasingly clear, for proper therapy depended upon differentiating between three possible major causes:*

COMMON CAUSES OF HYPERACTIVITY

(1) *Pain*.—Unquestionably, pain was present in many patients. This was due to burns, to irritation of mucous membranes, chiefly the eyes and the airway, by irritant gases, and to physical violence as a result of the panic that had occurred.

(2) *Fear and Hysteria*, as a result of the individual's experiences, appeared

to influence the behavior observed of those who had no injuries and doubtless were also a factor in the behavior of many of those with physical injuries as well. It will be recalled that this disaster occurred in a night club at about 10:15 P.M. Alcohol in some cases doubtless contributed to the excitement and the lack of self-control. The panic of the crowd and the physical pain and discomfort shared in producing the hysteria observed.

(3) *Anoxia*.—Cerebral anoxia is well known to give rise to excitement, occasionally to loss of self-control, and at times to manic behavior. This sequence is not infrequently encountered in chronic heart failure. Anoxia was probably a factor in our patients due to two main causes: (1) Interference with oxygen intake from obstruction of the airway was caused by a number of factors, for example, foreign bodies, chiefly vomitus. (This was a common hazard in the comatose but not in the hyperactive group.) Severe bronchial spasm occurred from pulmonary irritation caused by inspiration of the hot and noxious gases and probably interfered with the intake of oxygen. Edema of the airway developed into a problem beginning chiefly about four hours following the burns. How much of a lethal factor edema of the airway was in those who lived only a few minutes, is uncertain. (2) Impairment of oxygen transport by the blood was a factor in the development of anoxia largely as the result of the formation of carbon monoxide hemoglobin. Neither methemoglobin formation nor hemolysis as the result of encounter with noxious gases was a factor in our cases. While acute anemia must always be considered as a cause of cerebral anoxia, neither hemorrhage from associated wounds nor low blood pressure from shock was important here. In about one-third of the patients measurement of the blood pressure was not carried out because of interfering burned areas. Judging from other clinical signs these patients were not in shock. Where it was possible to measure blood pressure, two patients were found to have brief periods of hypotension; but frank surgical shock did not develop in any of the 39 patients.

THE THERAPY OF THE CAUSES OF HYPERACTIVITY

The importance of properly diagnosing the cause of the hyperactivity emerges from considerations of therapy. Moreover, a clue arises here as to the reasons for the often made recommendation of the use of enormous doses of morphine in burned patients. Occasionally large doses may be necessary; it appears probable in many cases that they are not only unnecessary but are in fact contraindicated. When the hyperactivity of the patients is caused by fear or hysteria or by cerebral anoxia the use of large doses of morphine is obviously unwise. *It seems probable that in burned patients morphine may often have been used in an attempt to treat conditions which will not respond favorably to morphine however large the dose.* An examination of the probable reasons for the use of large doses of morphine may throw some light on what is rational sedation for this group of patients.

IMMEDIATE THERAPY AFTER BURNS

PAIN

It has come to be accepted as a fact in medical practice that enormous doses of morphine must be used in the treatment of burned patients, doses that under normal circumstances might of themselves be fatal. Against this is the observation (Hardy, Wolff and Goodell¹) that the analgetic action of morphine increases rapidly up to 10 mg. ($\frac{1}{6}$ grain) intramuscularly, but is increased little by doubling or tripling the dose. While little of added benefit is obtained by this doubling or tripling, great increase in the toxic effects, particularly respiratory depression, results therefrom. It seems reasonable to question the advisability of the use of the customary large doses of morphine. Support for this view also emerges, as will be described below, from the realization that other factors besides pain may help to account for the hyperactive, even manic, behavior of individuals who have been subjected to a conflagration.

For pain, morphine administration is the treatment of choice. It must constantly be borne in mind that the common tendency in a disaster of this kind is to overmedicate. Safety depends upon the use of rather small divided doses repeated as necessary. Emphasis on these elementary matters may seem needless; but our experience was otherwise. For intravenous administration somewhat smaller doses are chosen than for subcutaneous or intramuscular use. Intravenous injection of the morphine is best—8 to 10 mg. ($\frac{1}{8}$ to $\frac{1}{6}$ gr.) doses are used. Such doses as these should be injected over 15 to 30 seconds, and may be repeated intravenously in about 15 minutes, until the desired effect is obtained. When many patients need treatment at once there will often not be time to administer the agent intravenously.

Whenever the subcutaneous or intramuscular routes of administration of morphine (or other agents) are considered, it must be borne in mind that under circumstances where the peripheral circulation is slow or inactive, the injected agent may not be absorbed. In patients coming from a fire, several conditions tend to reduce the peripheral circulation and, consequently, the rate of absorption of agents injected into the subcutaneous or intramuscular regions: Chilling from cold water spray and water soaked clothing (our patients had in some cases rectal temperatures as low as 94° F., pain and fear, and low blood pressure from various causes. Under circumstances such as these, agents injected into the subcutaneous or intramuscular regions will be absorbed very slowly if at all. Lack of attention to this possibility may result in repeated injection of the agent into these "refractory" patients. Later, when the peripheral circulation has been reestablished by shock therapy or warmth, the total injected dose may be absorbed at once with disastrous results.

When large numbers are to be cared for as quickly as possible, when the peripheral veins are collapsed, when slow absorption of the agent is desired, and, for various other reasons, subcutaneous or intramuscular use may be employed. Here 15 mg. ($\frac{1}{4}$ gr.) doses may be administered. In

such a case it is advisable to make up the solution (when a considerable number of patients must be treated rapidly) in a 20 cc. syringe with 15 mg. ($\frac{1}{4}$ gr.) per cc. concentration. A second such dose can be repeated in 20 minutes for a robust subject with severe burns. Increase in morphine medication beyond 30 mg. ($\frac{1}{2}$ gr.) is made only after one has assured himself that the need is for treatment of pain rather than fear or hysteria or anoxia. Even then, the justification in most cases for such large doses is questionable, as mentioned above.

If there is any possibility that large doses of morphine will be required it is advisable to use an extremity for their injection, and the site should be marked with a dye so that if signs of overmorphinization appear, absorption can be delayed by the use of a tourniquet above the site of injection. An unburned extremity should of course be chosen, for a tourniquet placed about one with peripheral burns would increase the edema formation in the injured area.

FEAR AND HYSTERIA

Fear and hysteria are best treated by repeated intravenous administration of a barbiturate, for example, sodium pentobarbital (nembutal) in 90 mg. (gr. 1.5) doses. In patients with pulmonary damage it is doubtful if more than two such doses should be given initially. While opinions are divided as to the wisdom of using paraldehyde in patients with injury to the lungs, there appears to be no serious objection to the use of small doses intravenously, as follows: Two or three cubic centimeters of paraldehyde may be injected over a half minute. One patient (Case 7) received paraldehyde, 4 cc. intravenously.

ANOXIA FROM AN INADEQUATE AIRWAY

Treatment of an inadequate airway takes precedence over all other forms of therapy. The following factors require consideration in this therapy:

The Removal of Foreign Material.—The Coconut Grove victims were either dining or had only recently finished dinner. Probably vomiting was more frequently encountered in this group than is usually the case in burned patients. Vomitus in the airway of the patients who arrived at the hospital either dead or in a moribund condition may have hastened some deaths. It is unlikely that such obstruction was present in the other, the hyperactive, group of patients. Occasionally, aspiration of the mouth and throat of these patients was carried out as a preventive measure.

Intratracheal intubation was carried out in three patients. In one of these cases it was necessary about two hours after admission.

It was considered to be life-saving in this case. Gross overdosage with morphine was present, and the intratracheal tube facilitated artificial respiration which was necessary intermittently over a five-hour period. In another case intratracheal intubation was used to facilitate bronchial aspiration several days after the accident. In the third case the procedure was used terminally to facilitate respiration preceding death. One or two other patients would have

IMMEDIATE THERAPY AFTER BURNS

received intratracheal intubation had they not been vomiting. It is usually unwise to introduce an intratracheal tube into a vomiting patient, for the necessary local anesthesia may permit the aspiration of vomitus. It is also unwise to insert an intratracheal tube surrounded by an inflatable cuff to prevent aspiration, for such inflatable cuffs have produced damage to normal mucosa of such degree that subsequent to their removal fatal local edema has occurred; therefore, we did not choose to use them in these subjects with already inflamed tissues. The best solution of this problem seems to be careful watching of all patients, with immediate tracheotomy in those that are vomiting when the airway shows signs of inadequacy.

Tracheotomy was required for the first time six and one-half hours following the fire. In all, five tracheotomies were carried out in the 39 patients during the recovery period. Three of the five patients died. The onset of serious edema of the airway in our cases, several hours after the burns, is in agreement with the history of other similar disasters, notably that of the Crile Clinic.

Treatment of Bronchospasm.—How great a rôle bronchospasm plays in the inadequate ventilation of the lungs in such patients is difficult to estimate. The bronchospasm was initiated presumably by heat or by the irritant gases breathed. It may have been a factor in precipitating or aggravating pulmonary edema formation. It was the consensus of opinion of those who examined the chests and roentgenograms of the patients that bronchospasm was a factor in producing the well-demonstrated peripheral trapping of air. Local edema, as well as foreign bodies, arising from sloughs in the bronchiolar walls were also doubtless involved in this. Attempts to treat this bronchospasm with epinephrine or ephedrine appeared to be quite unsuccessful. In a few cases the intravenous administration of 0.5 Gm. (7.5 grs.) of aminophylline appeared to be followed immediately by better ventilation and in some cases by cough, with the raising of sputum. This benefit may have lasted for only ten or fifteen minutes; estimation of this was difficult. Whenever injury of the airway has occurred, as in these patients, it is important to humidify the air breathed. All gases administered should be saturated with water vapor.

Oxygen Inspired.—Patients showing any signs of anoxia were immediately given by mask 100 per cent oxygen to breathe. In the first six hours seven of 39 patients required high oxygen concentrations. These were administered in order to get not only as full saturation of hemoglobin as possible through the damaged respiratory epithelium, but also to get the advantage of oxygen dissolved in the blood plasma. Subsequently, a total of 13 patients required oxygen therapy, chiefly by tent.

Increased Pressure in the Airway.—When oxygen is administered in a closed system under positive pressure, a greater diffusing surface is afforded the alveolar gases and the blood, and possibly the smaller airways are increased in diameter by the pressure, with the result that obstructing secretions are less effective in blocking the passages than they were. If this is the

situation, drainage might also be promoted by positive pressure. It is said that the use of positive pressure will prevent or curtail the formation of pulmonary edema. This seems to be open to question. Some believe, although incorrectly, that the partial pressure of the alveolar oxygen can be significantly increased by safe positive pressures. While this might be true at very high altitudes it is not true at ordinary atmospheric pressures. Notwithstanding the possible advantages to be gained from positive pressure we decided, rightly or wrongly, not to use it in these cases. In the first place, in a fairly wide experience with positive pressure in patients undergoing thoracic surgery it has been our observation that this procedure often lowers the systemic arterial pressure, probably by interfering with the passage of the blood through stretched out and narrowed alveolar vessels with the result that filling of the left heart is impeded. Positive pressure appears to interfere with carbon dioxide elimination. Finally, several patients exhibited a paradoxical pulse. We construed this to be a further argument against the use of positive pressure.

Helium.—When the tidal volume of air is normal or near normal it is unlikely that helium will be of value as a vehicle for oxygen, although it might be argued that if some bronchospasm is present the use of helium might be desirable. Our experience with helium in these cases was limited to a few trials of an experimental nature in which 75 per cent helium with 25 per cent oxygen was compared with 100 per cent oxygen. It was not possible at this time to make careful blood gas studies. We were not able to detect any improvement in the skin blood color with the helium and oxygen mixture as opposed to the high oxygen atmosphere. On the other hand, the pulse rates under the latter atmosphere were about 20 beats slower than when the helium and oxygen mixture was used (about 140 against 160). The difference in pulse rates suggests that oxygenation was better when 100 per cent oxygen was used than when the helium was employed.

ANOXIA FROM INADEQUATE TRANSPORT OF OXYGEN BY THE BLOOD

Carbon Monoxide Poisoning.—While many of the dead patients showed signs of carbon monoxide poisoning only two, questionably three, of our 39 living patients showed fairly definite signs of it. In these, attempts were made to eliminate the carbon monoxide by the administration of a continuous stream of oxygen containing five to seven per cent carbon dioxide. No rebreathing was permitted here. It is as desirable to give whole blood as soon as possible to these patients as it is to patients who may be anemic following hemorrhage or anemic from encounters with hemolytic gases in the smoke breathed.²

Shock.—When the patients arrived we supposed, incorrectly, that many cases of shock would develop. To combat shock, the intravenous injection of fluid was started on each patient within 15 minutes of the time of his arrival, in order to expedite the use of plasma as soon as it could be made ready. Both physiologic saline and five per cent glucose solutions were

IMMEDIATE THERAPY AFTER BURNS

used. The volume of these fluids administered was sharply restricted. From 200 to 500 cc. were administered before plasma was started or until the decision was made that intravenous fluids were not necessary. Twenty-nine patients received an average of 4.2 units (250 cc. unit) of plasma apiece in the first 24 hours. The variation was from one to nine units per individual in the first 24 hours. In the first seven days 147 units of plasma were administered. Also in the first seven days, 16 whole blood transfusions were administered for patients with reduced oxygen capacity of their blood.

As already pointed out, none of our patients developed frank shock. In the two instances in our cases where the blood pressure was low, even for a brief period, the head-down position was used; but as soon as the systolic arterial pressure had risen to 80 mm. Hg. we began gradually to reverse the position from head-down to head-up. Damage to the lungs must be assumed in patients such as these from the Cocoanut Grove even though it is not apparent. The head-up position reduces the pulmonary venous pressure and minimizes the tendency to edema formation in the lungs.

OBSERVATION OF PATIENTS FOLLOWING IMMEDIATE THERAPY

Factors of importance in the medical administration and organization of the treatment of large numbers of wounded individuals have been dealt with by Dr. Faxon in his accompanying article, and elsewhere by Faxon and Churchill.³ An indispensable part of the therapy of patients with burns of the airway is continuous and prolonged watchfulness of the respiratory and circulatory systems as well as of the patient's comfort. In the Cocoanut Grove disaster this was handled by the following personnel for dealing with our 39 patients.

Two physicians made rapid and continuous "chest" rounds on all patients following the initial treatment. It was their responsibility to watch the pulmonary ventilation, with particular attention to the development of pulmonary edema and to inadequate oxygenation of the blood from any cause. They called attention to deteriorating cases. They requested any new therapy needed, as intubation, oxygen therapy, etc.

Two men (medical students) made continuous rounds, determined blood pressures, pulse rates and recorded these data. One physician made "medication rounds," constantly looking for patients who needed further drug therapy, diagnosed the need and administered the appropriate agent. Constant watchfulness for overmedication is essential.

DELAYED REACTIONS

Delayed reactions are to be anticipated. Constant alertness must be maintained for the signs of (a) overmedication, particularly in cases where morphine may have been administered subcutaneously, with delayed absorption as in patients with poor peripheral circulation as a result of chilling or shock; (b) shock, as a result of plasma loss from burned surfaces, or other cause; (c) oropharyngeal, tracheal, or pulmonary edema; and (d) central nervous

system damage with delayed onset of cerebral edema with increased intracranial pressure.

Observations of the condition of the blood is of great help in guiding the care of these patients and in providing accurate quantitative data concerning the trend of delayed reactions. For example, the increased time required for a blanched area (made by the light pressure of a finger on the skin of the forehead) to fill in, often provides, in demonstrating the slowing of the peripheral circulation, a sharp warning of decline in the patient's circulatory condition, and of the possible approach of shock. The color of the blood must be maintained as near normal as possible. If assistants and equipment are available, hematocrit readings are obtained, for they are of great value as a guide to the need for whole blood or plasma. These were available by four and one-half hours (3 A.M.) following the accident. The determination of the plasma protein level refractometrically is a brief, simple procedure of value. In the days following the disaster more elaborate studies were possible. Helpful here were determinations (in arterial blood) of oxygen content and capacity. In one or two cases low oxygen values showed an urgent need for red cells. This might have been surmised some hours earlier had adequate attention been given to the low hematocrit values. Carbon dioxide content, plasma p_{H_2} , and plasma electrolyte values were helpful although not as important as the previously mentioned determinations.

NEED FOR FUTURE WORK

The Coconut Grove disaster called attention to the lack of information concerning the pulmonary lesions produced by fires and at the same time emphasized the need for study of this problem. For many years it has been known that pulmonary burns produced delayed effects in that, initially, victims appear to be in good condition and then rather suddenly develop respiratory impairment, obstruction, possibly bronchospasm and edema, and die. This was strikingly illustrated in the Crile Clinic disaster at Cleveland several years ago, and again recently here. Important gaps in therapeutic knowledge are concerned with (a) how best to overcome deficient gaseous exchange in the lungs arising from bronchospasm or caused by edema and by tissue sloughs; and (b) how to prevent these conditions. With the increase in flash-burns as a result of mechanized warfare, or for that matter mechanized civilization, therapy of the pulmonary lesions involved urgently needs study.

SUMMARY AND CONCLUSIONS

The patients who survived the Coconut Grove disaster long enough to receive therapy were in many cases hyperactive, even manic. Proper therapy depended upon correctly diagnosing the cause of this hyperactivity in a given case. Three major causes were: Pain; fear and hysteria; and cerebral anoxia.

Morphine is a useful therapeutic agent only for those in the first of these three groups. In the other two groups it is not only ineffective but is contraindicated in large doses. Although large doses of morphine are often

employed in treating patients from a conflagration, it seems probable that morphine may often have been used in an attempt to treat conditions which will not respond favorably to morphine irrespective of how large the dose.

In patients, who have been water soaked and chilled, who are frightened, or who are approaching shock, or whose peripheral circulation is otherwise greatly reduced, it is unwise to administer morphine (or other agents) subcutaneously or intramuscularly, for absorption will be either absent or greatly retarded. Lack of effect may lead to repeated administration of the agent in an effort to obtain an effect. Later, when the circulation has improved, the total of the subcutaneous injection may enter the circulation at one time with serious, even fatal consequences. Morphine should be administered intravenously to such patients. If, because of the great number of patients to be cared for, one cannot take time for intravenous administration of morphine, the agent should be injected into an unburned extremity and the injection site marked with ink, or a dye, so that if too great absorption of the agent is apparent later on, the inflow can be checked by means of a tourniquet.

For fear and hysteria, intravenously administered barbiturates are useful. For anoxia, arising chiefly from carbon monoxide poisoning, the treatment is seven per cent carbon dioxide in 93 per cent oxygen in continuous stream (without rebreathing) and with the administration of whole blood.

Various oxygen therapy technics (intratracheal intubation, tracheotomy, helium, positive pressure) are considered and reasons offered for discarding or employing them in treating the anoxia. The oxygenation problem is greatly complicated by severe bronchospasm and pulmonary edema. Consideration of these factors leads to a discussion of needs for future work.

REFERENCES

- ¹ Hardy, J. D., Wolff, H. G., and Goodell, H.: Studies on Pain: The Analgesic Action of Morphine and Codeine in Man. *Am. J. Physiol.*, 129, 375, 1940.
- ² Drinker, C. K.: Carbon Monoxide Asphyxia. Oxford University Press, New York, 1938.
- ³ Faxon, N. W., and Churchill, E. D.: The Cocoanut Grove Disaster in Boston. *J. A. M. A.*, 120, 1385-1388, 1942.

THE PULMONARY COMPLICATIONS: A CLINICAL DESCRIPTION

JOSEPH C. AUB, M.D., HELEN PITTMAN, M.D.,

AND

AUSTIN M. BRUES, M.D.

FROM THE JOHN COLLINS WARREN LABORATORY OF THE HARVARD CANCER COMMISSION AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON.

MANY BURNED patients have pulmonary lesions due to thermal or chemical burns of the lung, and an important part of burn management consists in the recognition and proper treatment of these pulmonary burns. This was particularly well emphasized in the Cocoanut Grove cases treated at this hospital, since all seven of the deaths were due to pulmonary complications. In fact, only three of the 39 patients were wholly free from respiratory symptoms, and they had covered their mouths with wet cloths or some article of clothing. A wet handkerchief appeared to have afforded adequate protection in one individual. There was little correlation between the severity of surface burns and the extent of pulmonary damage, and it was, therefore, necessary to watch for pulmonary signs even in those who were only slightly burned.

The first clue to the high incidence of pulmonary burns was afforded by the number who died within the first few minutes after reaching the hospital. They were very cyanotic, comatose or restless, and had severe upper respiratory damage. The surviving patients on arrival showed varying degrees of restlessness or excitement but soon became quiet following medication and removal to the ward. None was very cyanotic at this time; some were cherry-red in color, suggesting carbon monoxide inhalation. Most of them were burned about the mouth and nose, with singed nasal hair and reddening of the nasal mucous membranes. In general, the patients during the first three hours were breathing quietly and superficially, and coughing weakly. Chest examination at first showed distant breath sounds and this was associated with scattered basal râles in many cases. Several of the more severely burned victims were delirious, and two of these were quieted promptly by oxygen inhalation, suggesting that the delirium was due to anoxia aggravated by carbon monoxide poisoning and slowing of the respirations from morphine. Several patients, notably Case 25, soon became dyspneic, and progressed to a critical condition within a few hours.

About three hours after the fire, dyspnea suddenly appeared in others associated with cyanosis, restlessness, and increased râles. Since there was a rapid accumulation of edema in the external burns at this time, it is probable that burned pulmonary areas were undergoing similar changes. Thus, Case 25, who had shown early dyspnea but had remained quiet during the first three hours, became so short of breath that he insisted on getting on his hands and knees to facilitate breathing. An oxygen tent promptly

PULMONARY COMPLICATIONS OF BURNS

relieved cyanosis but had no effect on the dyspnea. Complications in this stage were (1) acute dilatation of the stomach in two of the most severely dyspneic patients; (2) a wildly delirious state, apparently due to anoxia; (3) auricular fibrillation in Case 2, eventually relieved by oxygen administration. This period of dyspnea subsided within a few hours.

A more critical period occurred about 24 hours after the fire and continued for the next 36. Dyspnea and cyanosis became much aggravated in certain patients, and râles again spread. This fulminating state was obviously due to edema from burns of the upper air passages, trachea and bronchial tree. Laryngeal examination had demonstrated reddening, edema, and burned areas extending beyond the vocal cords. Because of the critical nature of symptoms at this time, radical therapy appeared indicated and intubations and tracheotomies were done in several instances. Only two of the five treated by tracheotomy survived. In all, seven patients died. Necropsies on three indicated that the lesions had been too widespread to be relieved by these procedures even though additional oxygen was fed by catheter through the tracheal cannula. It is clear that an accurate estimate of the extent of a pulmonary burn cannot be made soon after occurrence, but it would appear that tracheotomy or tracheal intubation is indicated since it affords a chance of reducing the labor of respiration in a weakened patient by facilitating the passage of oxygen to the alveoli.

Whether phosgene or nitrous fumes were present in the smoke, as might be suspected from the delayed edema, apparently must remain a matter for speculation. Several of the patients exhibiting symptoms (Cases 5, 6, and 19) were exposed only to fumes and heat, and those for but a short period, and did not come in contact with flame at all. Case 13, on the other hand, had severe face and nasal burns, with denudation of her lower turbinate bones, but developed only slight lung complications. Professor Alan Moritz found carbon monoxide in a high proportion of those dead on arrival at the hospital, but no methemoglobin or porphyrin in the blood of the one patient tested. He is of the opinion that oxides of nitrogen were in the smoke, and it is noteworthy that the pattern of pulmonary reaction in the Cocoanut Grove survivors was not unlike that of the Cleveland Clinic fire.

Following subsidence of the epidemic-like attack of pulmonary edema, the final, subacute stage of pulmonary manifestations set in, of which the pathologic basis was diffuse bronchiolitis. This resulted in (1) obstruction of the air passages, particularly in the bases, sufficient to produce localized lobular collapse; and (2) trapping of air at the apices with acute emphysema. Both gave characteristic physical signs; the percussion note was highly resonant over emphysematous areas, and normal or slightly dull over the small areas of collapse, while the most striking finding was the surprisingly diminished breath sounds over the entire chest, most evident in the lower portions. Bronchial breathing was not heard except in Case 6, and at one time in Case 27. Râles, remarkably few in number were fine and crackling in the first few days and later coarse in character.

The absence of bronchial breathing suggested that the bronchi were plugged with secretion which prevented bronchial breath sounds from being transmitted to the periphery. This interpretation was borne out in many of the patients when the usual physical signs of pulmonary collapse disappeared after the coughing up of mucus and when similar signs appeared elsewhere. Thus, Case 20 had typical signs of collapse of the left lower lobe on the second day which disappeared on the next day after she coughed up a plug of pinkish-black material the shape of a medium-sized bronchus. On the fourth day, massive collapse of the other side was found to be present. The next day both lungs had cleared considerably, followed by appearance in the sputum of numerous brown plugs of mucus. A similar sequence occurred in Case 27 (who died on the third day). Postmortem examination confirmed these observations. The sputum raised by all who had lung involvement was of the same character, consisting at first of a heavy, tenacious mucus, later of a lighter, more frothy material. All of it was heavily stained with black particles resembling soot.

The areas of acute emphysema showed the same migratory tendency as those of atelectasis and lobular collapse. Here, too, auscultation showed that the breath sounds were almost absent and râles were rare but the emphysematous areas, which predominated in the upper lobes, were distinguished by their extreme resonance to percussion. Emphysema was also seen roentgenologically and at necropsy. The areas of collapse and of emphysema appeared to have a common origin in obstruction of the bronchioles—complete obstruction causing collapse, and partial obstruction producing emphysema.

Although breath sounds could barely be heard, the patients appeared to be breathing easily and with normal depth. As one might expect in this type of lesion the vital capacity of the lungs of most of the survivors (previously healthy adults) was markedly reduced, frequently to levels of only 800 to 1300 cc. The vital capacities in 19 patients averaged 73 per cent of the theoretical normal on the seventh day after the fire, with extremes of 25 and 120 per cent. Those which were diminished returned to normal only slowly. This diminished vital capacity is probably not unlike that found in cardiac decompensation. The lack of lung elasticity due to burns and edema probably accounted for it as much as the lung collapse and emphysematous areas. It doubtless was a factor in the anoxia experienced by these patients. The vital capacity test represents our best quantitative index of the severity of lung burns, even though it obviously cannot be used in the first few days after an accident.

Three patients, not previously afflicted with the disease, developed typical asthma. This was clearly present on the second day and persisted for over a week; then it disappeared, for the remainder of the hospital stay. They were relieved by steam inhalations and by adrenalin or by aminophylline several times, though the response was not invariable. This type of reaction can be described best by the reports of Cases 5 and 19. Other

PULMONARY COMPLICATIONS OF BURNS

patients with less obvious symptoms, but with asthma-like breathing, also obtained relief from the use of aminophylline. The response to these drugs indicated that the asthma was due in part to a muscular constriction of the bronchi, which could be relaxed, for it appears quite unlikely that the drugs would materially reduce the mucosal edema of the bronchioles. It is very interesting that intense asthmatic breathing could be precipitated by the bronchiolar lesions due to inhalation burns.

The lung complications encountered may be classified into four degrees of severity:

Grade 1: (9 patients.) This group showed minimal abnormal physical signs manifested by râles. There was no significant diminution of vital capacity, where it was estimated.

Grade 2: (8 patients.) The second group showed râles and emphysema; there was marked diminution in breath sounds together with roentgenologic evidence of trapping of air. There was slight diminution of vital capacity in all. (This grade is illustrated by Case 36.)

Grade 3: (7 patients.) The third degree of severity added persistent atelectasis, attributed to edema sufficiently marked to obstruct the passage of air into certain areas of the lungs during either phase of respiration. Vital capacities were reduced in varying degrees between the limits of 25 and 83 per cent of the theoretic normal. Cases 5, 6 and 19, who showed special features of interest, are described as examples.

Grade 4: (12 patients.) This group included the patients with the most severe degree of injury. Seven died (Case 27 is discussed). Five survived (Case 20 is described).

CASE REPORTS

Case 36.—This case illustrates Group 2 of lung complications—râles and emphysema. The patient retained consciousness throughout. On admission, he was cyanotic and there were burns of the mouth and nose. For 48 hours he was dyspneic. There were markedly diminished breath sounds over the right lower lobe and râles at both lung bases. He could phonate only in whispers. The roentgenogram showed a small area of atelectasis on the fourth day and later also evidence of some trapped air. After 12 days, his chest was clear except for occasional râles, but he was still raising a half ounce of sputum. His vital capacity, which was 58 per cent of normal six days after the fire, had risen to 79 per cent three days later. On discharge, after seven weeks in the hospital, there was no evidence by physical examination or roentgenogram of residual damage to the lungs.

Case 5.—This case illustrates Group 3 of the degrees of lung complications—râles, emphysema, and persistent atelectasis plus asthma. This man, whose mother has asthma, had never had any previous manifestation of allergy beyond slight exertional dyspnea with chest colds; he had a heavy cold at the time of the fire.

He was admitted unconscious and cyanotic, with burns of the lips, mouth, nares, tongue, and trachea. There were râles in both chests. Twenty-seven hours after admission, his breathing became much more difficult, and was relieved following intravenous aminophylline. This was interpreted as bronchial spasm superimposed upon bronchial edema. The asthmatic breathing persisted for four days, and râles, with suppression of breath sounds, for eight days in all. Roentgenograms showed air trapping and atelectasis. His vital capacity rose from 54 per cent of normal on the sixth day to 69 per cent three days later.

This patient was seen one month after the fire, at which time there was complete freedom from symptoms together with a normal roentgenogram.

Case 6.—A female, age 16, well except for previous sinusitis. In the fire she lost consciousness, and awakened in the hospital, nauseated and vomiting. On entrance, no râles were heard in the lungs, though the nares, mouth, and pharynx showed evidence of the effect of the heat. She was not otherwise much burned, but was in mild shock, the systolic pressure falling from 120 to 80 mm. Hg., which was improved by a plasma transfusion. Within three hours, she developed hoarseness, with moist râles throughout both chests, signs of consolidation in left lower lobe, and showed marked cyanosis and an elevation of respirations to 40 per minute. She was much improved in color and breathing by oxygen, by Boothby mask, after aminophylline had failed to relieve her. However, she became more restless, raised tenacious mucus, and 12 hours after the fire she was put in an oxygen tent because of her poor responsiveness, cyanosis, and increasing respiratory difficulty. She had to breathe oxygen-rich mixtures nearly continuously until the evening of the fifth day.

Prior to the third day, physical signs indicated transient blocking of the large bronchi, but thereafter there remained a constant block of the lower portion of the left lower lobe where constant dullness to percussion and bronchial breath sounds were heard (unique in this series). The rest of the chest examination showed constant and marked diminution of breath sounds with variable and migrant areas of râles, dullness, and hyperresonance though collapse of the right lower and emphysema of right upper lobe were usually found. She could exert no force on expiration or cough and could not dislodge the mucus plugs in her bronchi.

She gradually improved until the eleventh day, when it appeared safe to tip head and chest to drain the lung. This had a remarkably good and rapid effect, and though she raised no sputum the lung collapse in both lower lobes disappeared; aeration thereafter was much improved and the diaphragms descended well for the first time. Her vital capacity rose immediately from 0.8 liters (25 per cent theoretic normal) to 1.2 liters (37 per cent of normal), and by the end of the third week this had returned to 3.0 liters, or 90 per cent of normal. Her convalescence was uneventful.

Case 19.—A male, age 42, with no previous history of asthma or chronic cough, was largely a problem of inhalation burns, with minor burns particularly evident in the nose and mouth. On entrance, he had râles in both lung bases followed, six hours after the fire, by signs of blocking of his right lower lobe. Six hours later he had asthmatic breathing and moist râles and expiratory stridor, mostly in right upper lobe. After 29 hours, he became very ill, with intense dyspnea, evidence of obstructed bronchus of right lower lobe, and universal râles; and later, signs of emphysema in right upper lobe. Tracheotomy was considered but not done. Asthmatic breathing from the beginning was relieved by aminophylline. On the third day, he could not phonate audibly and local examination disclosed diffuse swelling and redness throughout the nasopharynx, with chest signs of diffuse emphysema sufficient to depress the diaphragm and obscure the heart. The breathing was typically asthmatic and the clinical picture consistent with asthma of long standing. The patient was very ill, required repeated stays in an oxygen tent, and was frequently relieved by aminophylline and codeine as well as by adrenalin injections. This continued with gradual improvement, with increasing amounts of mucoid sputum (containing 1.8 Gm.% protein) and lessening of asthmatic breathing and physical chest signs. The vital capacity was greatly reduced by the expiratory push-test (see Schatzki) and after ten days was 1.4 liters, only 34 per cent of the theoretic normal and 74 per cent of normal by the nineteenth day. At the end of a month the lungs still sounded far from normal. There was no dullness to percussion, but breath sounds were very distant and faint over the whole back, most marked down the right lower lobe. Many coarse bronchial râles were heard over the left lower lobe, particularly after coughing. Vital capacity was 2.6 liters, or 65 per cent of

PULMONARY COMPLICATIONS OF BURNS

theoretic normal. The patient felt weak but well, complained of no asthma or shortness of breath, and only of the persistent cough and sputum.

Case 27.—A female, age 18, was very seriously burned. On admission, her color was slightly cherry-red, and she was wildly delirious. After an hour she developed respiratory failure; she was given artificial respiration followed by oxygen and carbon dioxide; an airway was inserted and she was then put into an oxygen tent. One hour later her lungs were wet, her systolic blood pressure varied from zero to 120; she was unresponsive, and six hours later she was still unresponsive. Her lungs were full of râles. Given aminophylline, she awakened and coughed, and repeated tracheal aspiration produced a 7 cm. bronchial cast streaked with black pigment. Roentgenograms 11 hours after admission, showed partial collapse of the right upper lobe and probably of the middle lobe. There was also acute dilatation of the stomach and esophagus. The next roentgenogram, after a four-hour interval, during which a Levine tube had been used, showed that the dilatation of the stomach had decreased and the esophagus was no longer dilated.

The next morning her breathing was labored, almost Cheyne-Stokes in character, and a patch of bronchial breathing was heard at the base of the right lung. An electrocardiogram showed sinus tachycardia, with a rate of 150; the tracing was otherwise within normal limits.

She continued to have a good airway for a day, then developed gurgling noises in her trachea. Suction with an intratracheal tube evacuated a very thick mucus, but it could not all be removed. The patient became cyanotic and died 62 hours after admission. An autopsy was performed.

Case 20.—This case represents the most severe grade of lung complications encountered among the survivors. This patient, a female, was one of those who were badly burned, and her dressings made examination of the chest unsatisfactory. She was cyanotic and had râles on admission, but did not begin to cough until about 24 hours later. During the next few hours she sounded like an asthmatic, until she coughed up a plug of pinkish-black material, which suggested a bronchial cast. On the third day following the fire, she developed a massive collapse of the right lower lobe. Laryngoscopy showed definite edema of the cords and a tracheotomy was performed. That evening she was unconscious and had a respiratory rate of 38 in her oxygen tent. The lung collapse diminished in the course of about 24 hours, though localized areas of atelectasis remained for 20 days. During the period of reexpansion she produced many brown mucoid plugs.

She improved gradually. The tracheotomy tube was removed after 29 days. Scattered wheezes, clearing after deep breathing, were heard for some days more. A roentgenogram, in the eighth week after the fire, showed no evidence of any abnormality.

The sequence here was partial bronchial obstruction due to a plug, associated with clinical asthma. Subsequent complete plugging produced massive collapse. The patient survived this acute phase and the bronchial edema subsided. As laryngoscopy showed only edema and no third-degree burn of the cords, it is improbable that she had a deep burn of the bronchial mucosa. Seven weeks after the fire her lungs were apparently normal, as determined both by physical and roentgenologic examination.

Therapy for severe lung complications of burns is difficult and in a sense inadequate, but it is important that it be carried out vigorously and with a clear conception of the underlying pathology. At first, the problems are essentially those of getting sufficient oxygen to the lungs, of reducing edema of the mucous membranes, and of avoiding pulmonary infection. Oxygen in high concentration is the obvious emergency therapy. Patients

receiving morphine should be watched closely. Although intubation and tracheotomy were not highly successful in our cases, we believe that they fulfill a definite function in relieving labored breathing and in facilitating the delivery of oxygen, and should be resorted to in patients with acute cyanosis and in those with severe upper respiratory lesions. Intravenous saline solution is contraindicated since it will increase edema and exudate in the bronchial tree; plasma transfusions will apparently not do this if given in moderate amounts, and obviously they are the essential therapy after burns. It should be remembered that loss of fluid from burned areas of skin and superficial edema can occur with little harm, while similar occurrences within the respiratory tract may be dangerous.

It is, of course, most important to avoid infection. None of the patients in this group developed pneumonia or pulmonary abscess, and this was in all probability due to their isolation on one floor and the precautions taken to avoid cross infections by the continuous use of masks and gowns, and by scrupulous cleanliness. The early use of sulfadiazine was probably also an important factor.

In the later subacute phase, the main problem was to lessen the viscosity of the sputum and to liberate blocked bronchi. A moist atmosphere, produced by means of steam kettles and by liberating steam from the room heating units, gave considerable comfort and improved breathing. Aminophylline appeared helpful, not only in the asthmatics but also in the other dyspneic patients. To loosen secretions, ammonium chloride appeared to be of some value. Gravity drainage during convalescence had a dramatic effect in liberating one collapsed lung (Case 6), and should be used when the patient is well enough to endure it.

CONCLUSIONS

Of the numerous lessons to be learned from these lung burns, the following should be emphasized: (1) That covering the mouth with a wet cloth may afford complete protection against pulmonary burns; (2) that in most patients the degree of inhalation burn was by no means ascertainable directly after the fire, and the extreme edema, which occurred later could not be predicted; (3) the resuscitation of patients in acute attacks of edema was difficult and unsatisfactory, and these acute attacks must be watched for with great vigilance, even in patients with minimal surface burns.

The pulmonary complications were bizarre and characterized by extreme variability, with areas of lung collapse and emphysema, which were often quite transient and migratory. As the injury to the bronchioli healed, these signs disappeared and the lungs sounded as though no permanent damage had occurred. Roentgenologic examination confirmed this, but only time will tell whether bronchial scars will constrict and produce bronchiectasis in the future.

ROENTGENOLOGIC REPORT OF THE PULMONARY LESIONS

RICHARD SCHATZKI, M.D.

FROM THE DEPARTMENT OF RADIOLOGY, MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

IN the first 12 hours the rôle of the Roentgenologic Department in regard to the Cocoanut Grove disaster seemed to be that of an observer. This impression was caused primarily by the surprising absence of fractures among the survivors of the fire. In fact, only in two of these was there enough clinical suspicion to warrant any roentgenologic examination, and in neither of these was a fracture found.

The first roentgenologic examination of the lungs was made on the morning following the disaster, that is, 12 hours after the beginning of the fire and approximately 10 to 11 hours after patients had reached the hospital. By this time it had become apparent that the majority of the survivors were suffering primarily from some pulmonary complication, the nature of which was not clear. Test films, with a portable machine, were taken on a few selected patients. A bizarre appearance of the lung fields was noted in most cases, while the lungs appeared normal in others. Clinically unsuspected, marked dilatation of the stomach was found in several of these chest films. The results of the trial examinations seemed important enough to justify continuing the studies on a more extensive basis.

The roentgenologic investigation began under severe handicaps: A great proportion of the patients was seriously ill; some were unconscious; and most were extensively bandaged. All examinations had to be performed on the ward, which had become an Isolation Ward. During the first 24 hours a portable machine (10 m. Amp.) was used for the radiographic work. On the second day following the disaster, November 30, a mobile condenser discharge unit (General Electric) with a capacity of $\frac{1}{4}$ mfd. was set up in one of the sun parlors on the ward and was left there for the duration of the isolation period. The patients were wheeled in their beds to this room and radiograms at six feet distance were thus obtainable, except in the cases of a few very sick patients.

The importance of the films taken at inspiration and expiration was soon realized, and all examinations, therefore, included both phases of respiration. Lateral films were taken only in exceptional cases and were not very successful due to technical difficulties.

Thirty-nine cases were admitted to the hospital ward. Four of them were discharged before a roentgenologic examination was made (Cases 3, 21, 24 and 31). The remaining 35 patients had one, and most of them repeated, roentgenologic studies of the chest. It showed evidence of pulmonary pathology at some time in 22, whereas the examination of the other 13 was negative at all times.

The roentgenologic appearances were bizarre and changed from patient

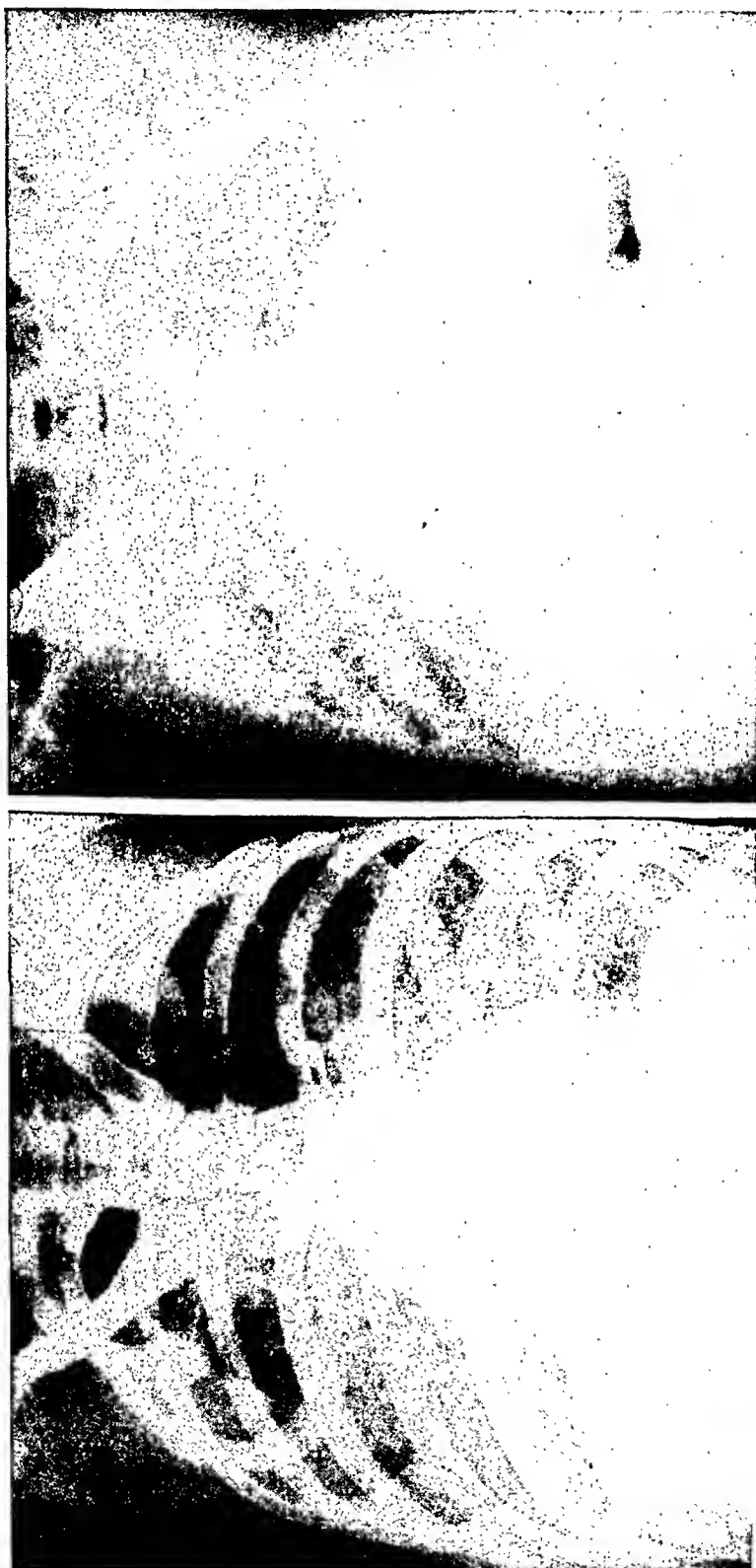


FIG. 8.—Postmortem films taken on two victims of the fire who were dead on arrival at the hospital. The lungs in both cases show extensive pulmonary edema, which was confirmed at autopsy.

X-RAY OF PULMONARY LESIONS

to patient. Flame-like areas radiating asymmetrically from one or both hili, bands and lines of increased density, large homogeneous and small military areas of increased density were found, as well as areas of increased brightness. In general, the pictures presented were quite puzzling. Some of the lesions were obviously produced by bronchial obstruction, while the significance of others was doubtful. The further development of the roentgenologic changes, as well as the anatomic findings in the few cases which came to autopsy, clearly showed that interference with aeration due to complete or partial obstruction of the bronchi, and particularly of the smaller bronchi, was the cause of most, if not all, visible pulmonary changes.

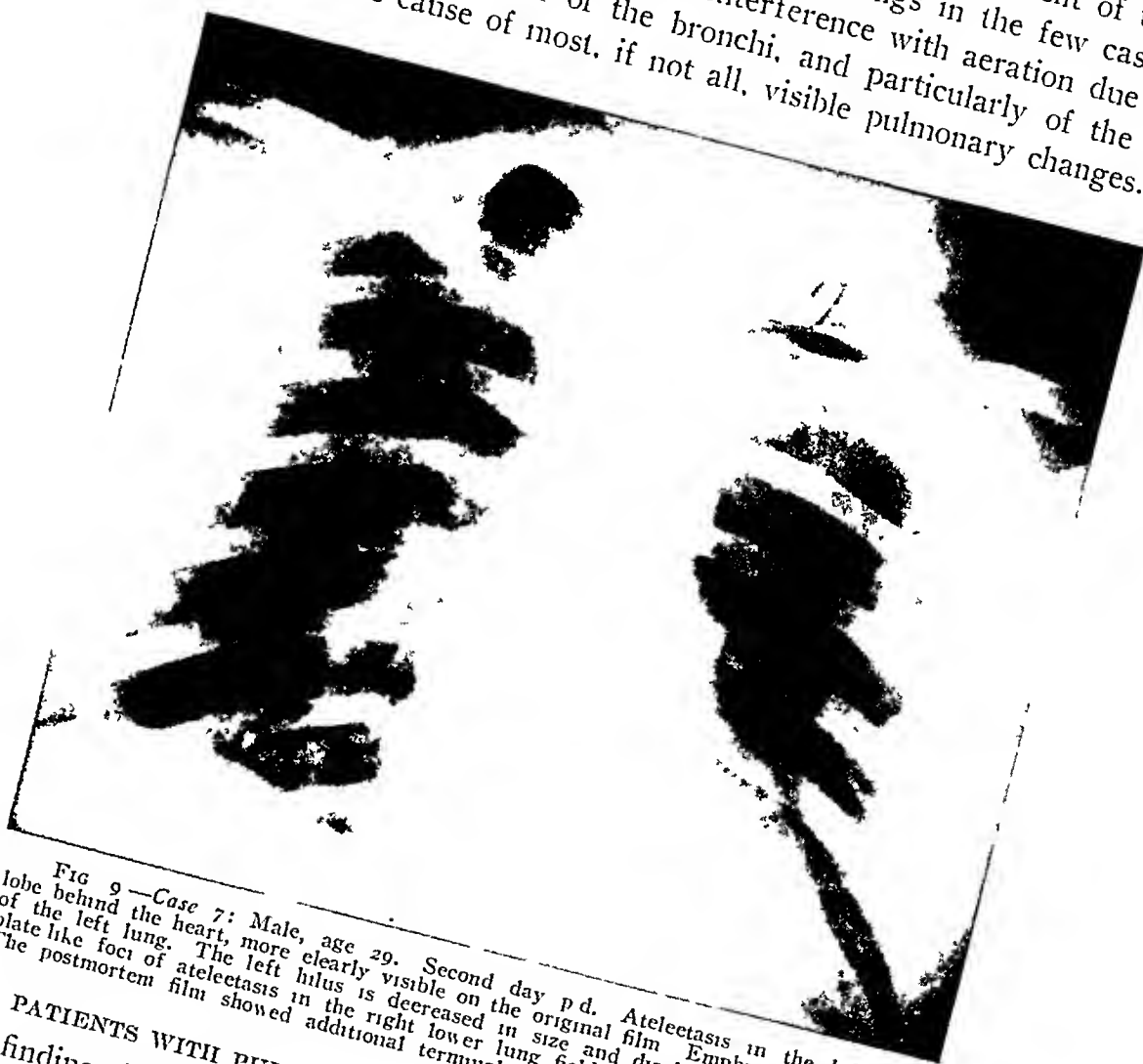


FIG 9—Case 7: Male, age 29. Second day p.d. Atelectasis in the left lower lobe behind the heart, more clearly visible on the original film. Emphysema of the rest of the left lung. The left hilus is decreased in size and displaced downward. Small plate like foci of atelectasis in the right lower lung field. Patient died 11 hours later. The postmortem film showed additional terminal pulmonary edema. Autopsy.

PATIENTS WITH PULMONARY PATHOLOGY BY ROENTGENOGRAM

The findings in the autopsied cases will be described first before analyzing in greater detail the various roentgenologic changes.

Roentgenologic Findings in Two Autopsied Cases Dead on Arrival
Only two of the victims of the disaster, dead on arrival at the hospital, had roentgenologic examination of the chest. Both cases showed extensive, diffuse, poorly defined haziness extending throughout the greater portion of both lung fields and having the characteristic roentgenologic appearance of pulmonary edema (Fig. 8). The presence of pulmonary edema was con-



B

A

FIG. 10.—Case 27: (A) First day, 12 hours p.d. Extensive areas of atelectasis in the right lung field; marked dilatation of the stomach and of the air-filled esophagus, which is visible to the right of the dorsal spine. Trapped air in a localized round area superimposed on the right hilus just below the safety pin. (B) Twenty-four hours later. Increase in the areas of atelectasis on the right side; new areas of atelectasis and emphysema on the left side. The localized area of trapped air is still visible in the right hilus.
Clinical Data: Female, age 18. Severe inhalation burns and extensive burns of face, back and extremities. Chest full of rales; rapid respiration, becoming labored on the second day p.d. Death 28 hours following the last film (Fig. 3B). Autopsy.

X-RAY OF PULMONARY LESIONS

Fig. 11.—Case 33. Patient died 13 hours p.d. Film taken immediately after death shows mottling of both lung fields, particularly marked on the right side.
Clinical Data Male, age 43. Fifty per cent bedsores, burns. Lungs coarse, most tales and prolonged expiration. No autopsy.

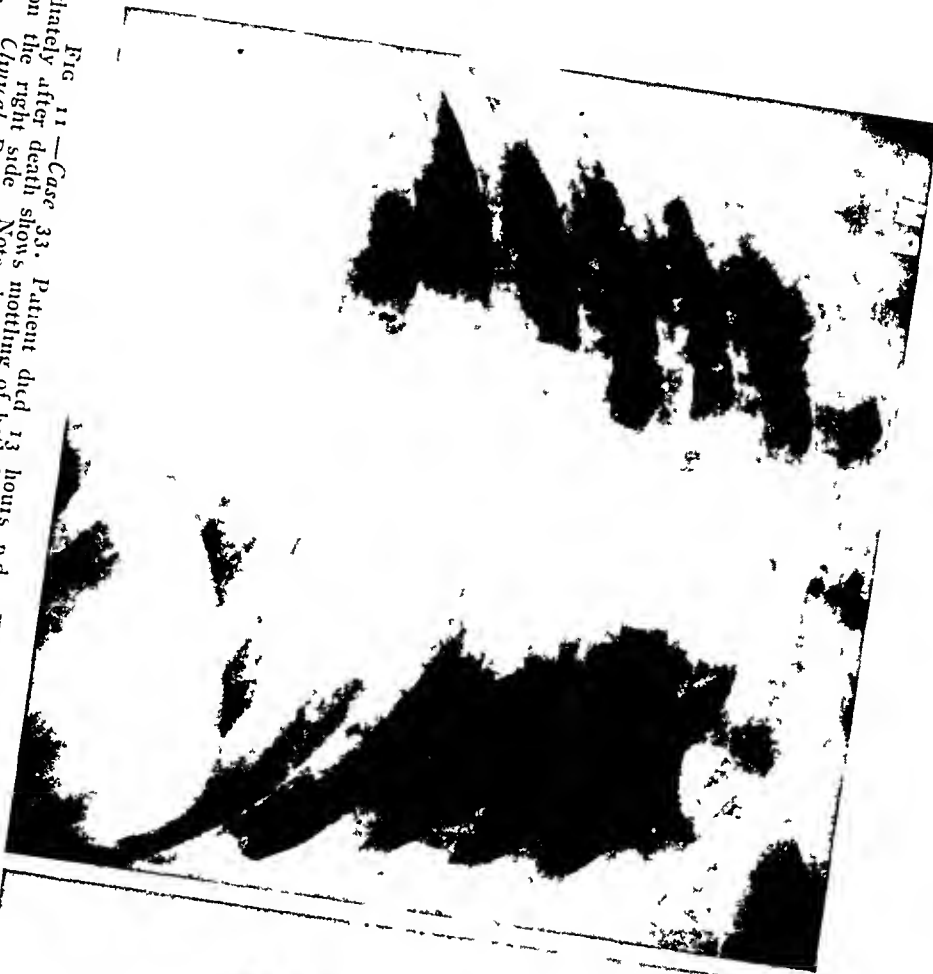
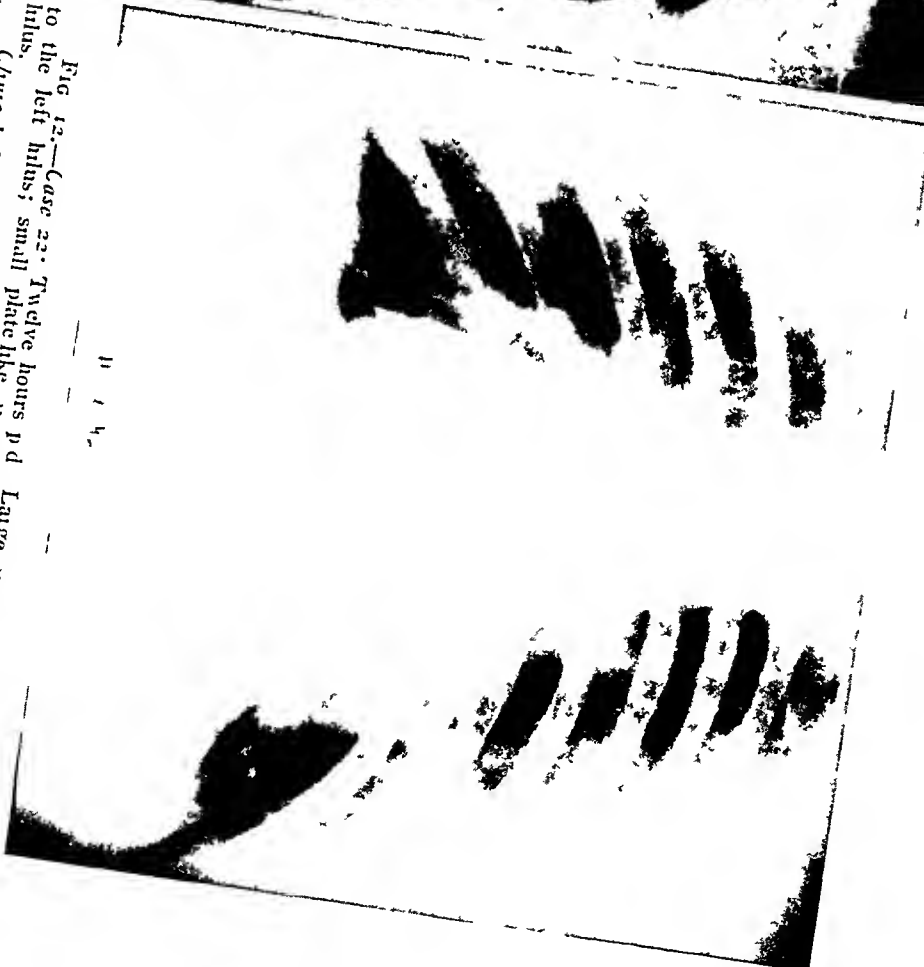


Fig. 12.—Case 22. Twelve hours p.d. Large area of atelectasis close to the left hilus; small plate-like area of atelectasis close to the right hilus.
Clinical Data Male, age 39. Severe inhalation burns, extensive to the face, neck, shoulders and hands. Patient died 11 hours after roentgenologic examination. No autopsy.



firmed by autopsy in both cases. The roentgenologic appearance, as well as the findings at autopsy, was quite different from that seen in patients who survived the first 12 hours; in none of the latter cases was extensive pulmonary edema seen. The blood in the two patients dead on arrival showed a high carbon monoxide saturation—42 and 50 per cent, respectively. Whether this, or another cause, was responsible for the pulmonary edema remains a question, but it is very unlikely that the pulmonary edema in these two cases was similar in origin to the pulmonary changes found at a later date in the survivors.

*Roentgenologic Findings in Three Autopsied Cases which Died
in the Hospital*

On only three of the seven patients who died in the hospital were autopsies performed. All three had roentgenologic evidence of pulmonary pathology.

Case 7.—In addition to other burns, this patient had burns of the face and severe inhalation burns. A film taken 36 hours after the disaster* showed emphysema of the left upper lung field, with questionable collapse within the left lower lobe. Another film, taken six hours later, demonstrated more conclusively the atelectasis within the left lower lobe in addition to the emphysema. There were also small plate-like foci of atelectasis in the right lower lung field (Fig. 9). The patient died the morning of the third day, 53 hours p.d.* A postmortem film showed pulmonary edema and evidence of trapped air in the left lung. *Autopsy.*—Tracheitis, bronchitis and bronchiolitis: Areas of atelectasis with hemorrhage, possibly representing early infarction, the largest area in the left lower lobe, and some pulmonary edema. (See Dr. T. B. Mallory's report for details)

COMMENT.—A patient with marked inhalation burns showed early evidence of emphysema and atelectasis, confirmed by autopsy. The changes were adequately explained by severe bronchiolitis. In addition, there was possible evidence of infarction of the collapsed areas, probably secondary in nature. The pulmonary edema was terminal, and in all probability not specifically connected with the underlying pathology.

Case 25.—Severe inhalation burns; gurgling and cyanotic. Temperature 103°–104° F. The first film of the chest, taken 12 hours p.d., showed localized increased density in the left lower and middle lung fields, which at that time was thought to be pneumonitis or pulmonary edema, but which was later explained as an area of atelectasis. A film taken 29 hours later showed no appreciable change. The patient died 42 hours p.d. Postmortem film showed emphysema of the left upper lobe and peculiar, well defined mottled areas throughout the right lung, and less pronounced on the left side. *Autopsy* showed extreme membranous tracheitis, bronchitis and bronchiolitis; anatomic emphysema; focal areas of atelectasis; and some pulmonary edema. (See Dr. Mallory's report for details)

* For convenience, and to avoid repetition, the abbreviation "p.d." will be used instead of the words "after the disaster."

X-RAY OF PULMONARY LESIONS

Fig. 13.—Case 6 (See also figures 14-16 on same case): This case shows the development of extensive, long-standing collapse of both lower lobes. (A) Twelve hours p.d. Small, minimal amount of atelectasis seen through the heart shadow. Note the downward displacement of the left hilus. (B) Twenty-four hours later. There is now a large area of

A

B



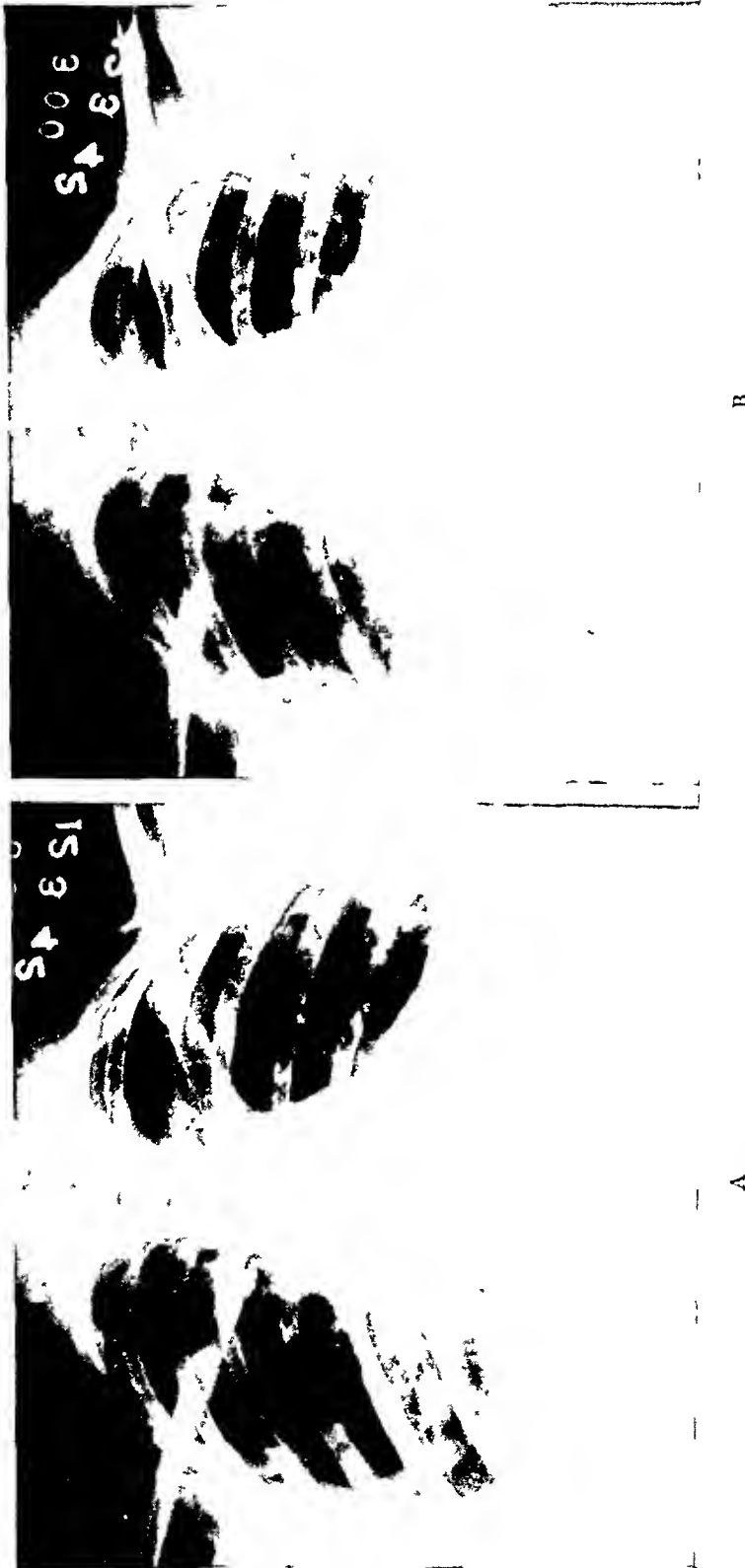


FIG 14—Case 6 (Continued) Fifth day p d There is now extensive collapse in both lower lobes. It became evident on the third day p d, and had not appreciably changed since. Note the high fixed diaphragm. (A) Inspiration. (B) Expiration.

X-RAY OF PULMONARY LESIONS



Fig. 15.—Case 6 ((continued): Thirteenth day p d. The collapse of the lower lobes has improved and there is some motion of the diaphragm. (A)

A

B

COMMENT.—Areas of atelectasis and emphysema were present on the first film taken 12 hours p.d. The peculiar mottling of the lung seen in this case and in one other fatal case (Case 33) (Fig. 11) could be explained either by the demonstration of the exudate-filled small bronchioles or by multiple small areas of atelectasis.

Case 27.—Severe inhalation burns, in addition to other burns. Chest full of râles. Films taken 12 hours p.d. (Fig. 10 A) showed extensive plate-like areas of atelectasis in the right upper lung field with elevation of the right hilus. Below this region there was a peculiar flame-like area of increased density. A definite circular 4-cm.-area of increased brightness was superimposed upon the right hilus. The stomach was markedly dilated and air-filled, as was the esophagus. Film taken five hours later showed the stomach and esophagus no longer dilated (the air had been aspirated). The flame-like process in the right midlung field had increased in extent. Films taken 29 hours p.d. showed disappearance of the atelectasis in the right upper lobe, and slight decrease of the process in the right middle lung field. At this time, there was markedly increased density in the right lower lung field. Films taken 35 hours p.d. showed no appreciable change on the right side; but there were definite areas of increased density close to the left hilus as well as in the left lower lung field. There were some emphysematous changes on the left side (Fig. 10 B). The patient died 63 hours p.d. *Autopsy* showed severe tracheitis, bronchitis, and bronchiolitis, with patchy areas of atelectasis and emphysema in both lungs: Areas of early pneumonia, probably not older than 24 hours: A few small areas of early or partial infarction (See Dr. Mallory's report for details).

COMMENT.—This case shows particularly well the bizarre roentgenologic appearance of some of the atelectatic areas as well as the rapid change in their amount and location. Infarcts may have been responsible for a few of the roentgenologic changes. A perfectly round area of localized emphysema existed in the right middle lung field. It had the appearance of trapped air as sometimes seen in children's pneumonia (pneumatocele).

ANALYSIS OF THE ROENTGENOLOGIC FINDINGS

As mentioned before, the roentgenologic findings in the victims of the disaster varied from patient to patient, and often in a given patient from day to day. The resulting pictures were peculiar, the published illustrations giving only an incomplete impression of the variety and combinations. An analysis of the manifold appearances, however, shows that the majority of the changes can be explained by the presence of various degrees and amounts of (1) atelectasis and (2) emphysema, both apparently due to bronchial obstruction. These two types of lesions represent the vast majority of the changes. In addition, there are in a few cases other abnormalities, the nature of which is less clear, which will be described here as (3) areas of miliary mottling; and (4) areas of diffuse density without decrease in size of the involved portions of the lung ("drowned" lung). The four types will be discussed in the following paragraphs.

Areas of Atelectasis

Sudden, massive lobar collapse, comparable to postoperative collapse,

X-RAY OF PULMONARY LESIONS



A

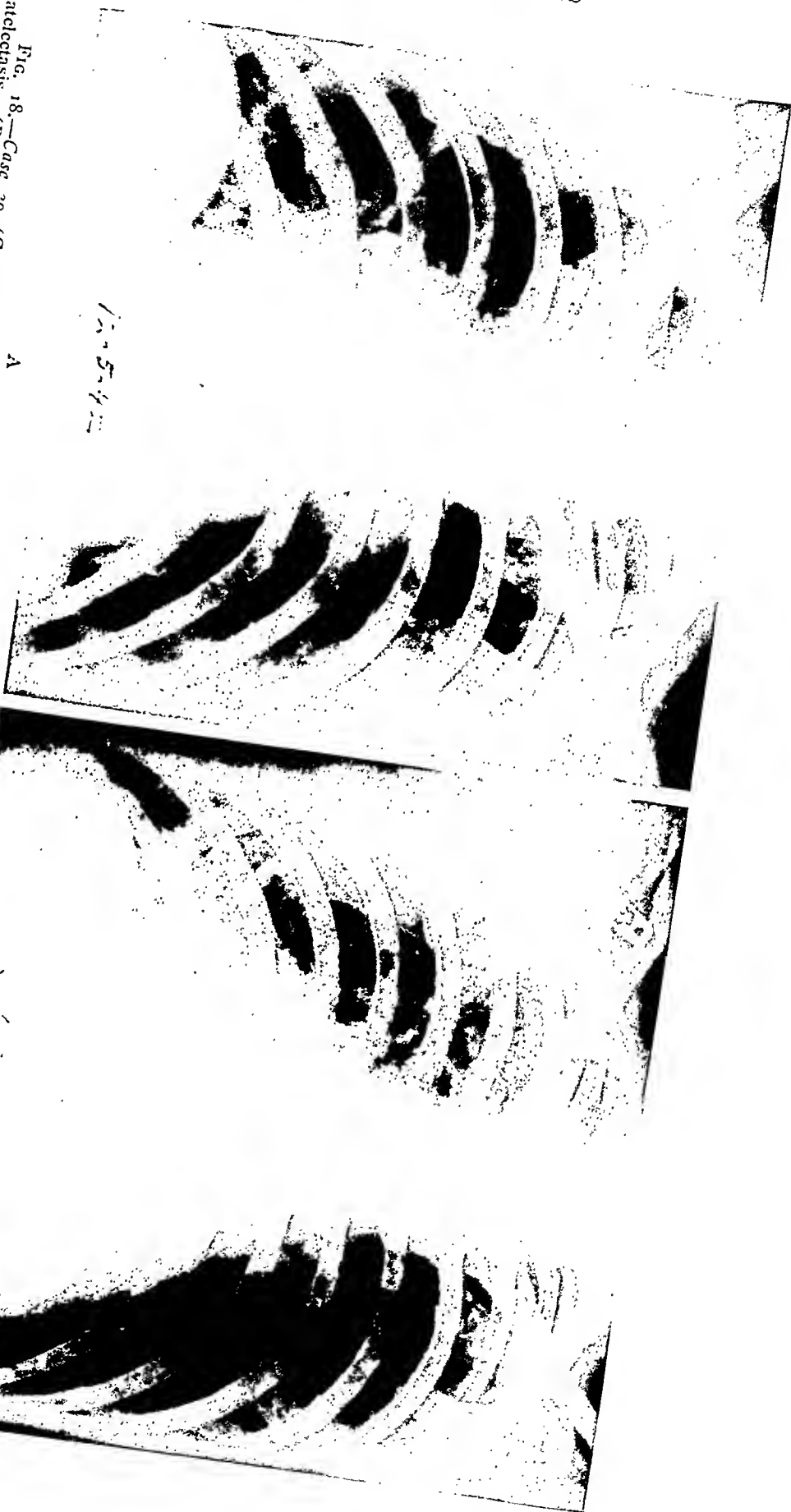
B

Fig. 16.—Case 6 (Continued). 10th week, p.d. The collapse of the lower lobes has almost completely disappeared. The left hilus is still slightly lower than normal. The diaphragm shows marked improvement in respiratory motion (A) Inspiration. (B) Expiration. The left hilus is still slightly throughout the first few days p.d. Marked inhalation burns; only minimal skin burns. Early respiratory embarrassment which was quite striking any evidence of pathology either roentgenologically or clinically (For further details see Dr. Aub's report)



FIG. 17.—Case 20: (A) Third day p.d. Heavy density in the left lower lung field without decrease in the size of the involved lobe ("drowned lung"). (B) One day later. The pathology in the left lower lobe has disappeared and there is now massive collapse of the right lower lobe. (See Figure 18 for clinical data)

X-RAY OF PULMONARY LESIONS



A

B

Fig. 18.—*Case 20* (Continued): (A) Seventh day p.d. The massive collapse of the right lower lobe has disappeared, leaving plate-like areas of atelectasis. (B) Eleventh day p.d. Reappearance of the collapse of the right lower lobe with mottled areas of atelectasis in the right upper lobe and thick, tenacious sputum, and had many coarse rales, especially expiratory wheezes. Tracheotomy on 3rd day. On the 4th day (Fig. 17B) the patient improved. Roentgenologically, the massive collapse of the right lower lobe had disappeared but there was a later relapse (Fig. 18B). Eight weeks p.d. there was no evidence of pulmonary pathology either clinically or roentgenologically.

was seen in one patient only (Case 20) (Fig. 17 B). It was obviously produced by obstruction of a large bronchus. Gradual complete collapse of both lower lobes was seen in another patient (Case 6) (Figs. 13, 14, 15 and 16). More commonly, the obstruction was in smaller bronchi and resulted in collapse of the corresponding lobules, usually visible as triangles or bands of increased density (Figs. 10 and 23 A). Often the small areas of atelectasis were visible as fine lines only, representing disk-like areas of atelectasis seen edge-on (Fleischner's⁵ lines). They ran horizontally, obliquely, and in the lower lobes even vertically through the lung fields (Figs. 21 and 22 B). In addition to the autopsy findings, there were several roentgenologic factors which proved the atelectatic character of these lesions. If they were extensive, the noninvolved parts of the lung on the same side showed compensatory emphysema. The diaphragm was commonly elevated on the involved side. Most characteristic were the changes in position and size of the hilar shadows, which were displaced up or down towards the atelectatic lobes, and were smaller on the involved side. In many instances these hilar changes were the first clue towards finding small areas of atelectasis.

A lateral shift of the mediastinum was rarely seen, apparently due to the frequent bilateral pulmonary involvement.

A connection between the roentgenologic findings and bronchial obstruction was demonstrated early by the use of a simple clinical test—the study of the expiratory “push” (forceful expiration with open mouth against the examiner's palm) (Volhard¹¹). No stream of air could be felt in patients with marked pulmonary changes, and in others the stream was diminished. The expiratory “push” improved parallel with the roentgenologic clearing of the lungs. This parallelism was later confirmed by more exact studies of the vital capacity.

The majority of the roentgen-positive cases had localized areas of atelectasis at one time or another. Usually, several of these were present (Fig. 21), at times only one or two. While atelectasis was demonstrable in most of the severely damaged cases on the first day p.d., this pathology was not seen in other cases until the second day p.d., sometimes not before the third and fourth day. In one patient (Case 13), only localized emphysema was demonstrable for a period of ten days, when the first evidence of atelectasis was present in the same region. In some instances, the areas of atelectasis changed from day to day. Usually, however, the same areas of atelectasis remained visible until the process had cleared up. In most cases the pulmonary pathology disappeared within the first two or three weeks; in a few cases it was demonstrable at a later date, up to four or five weeks; and in one case, a small area of atelectasis still existed 17 weeks p.d.

Chart I shows the time of appearance and disappearance of the areas of pathology and also indicates how long after the disaster check-up films were taken.

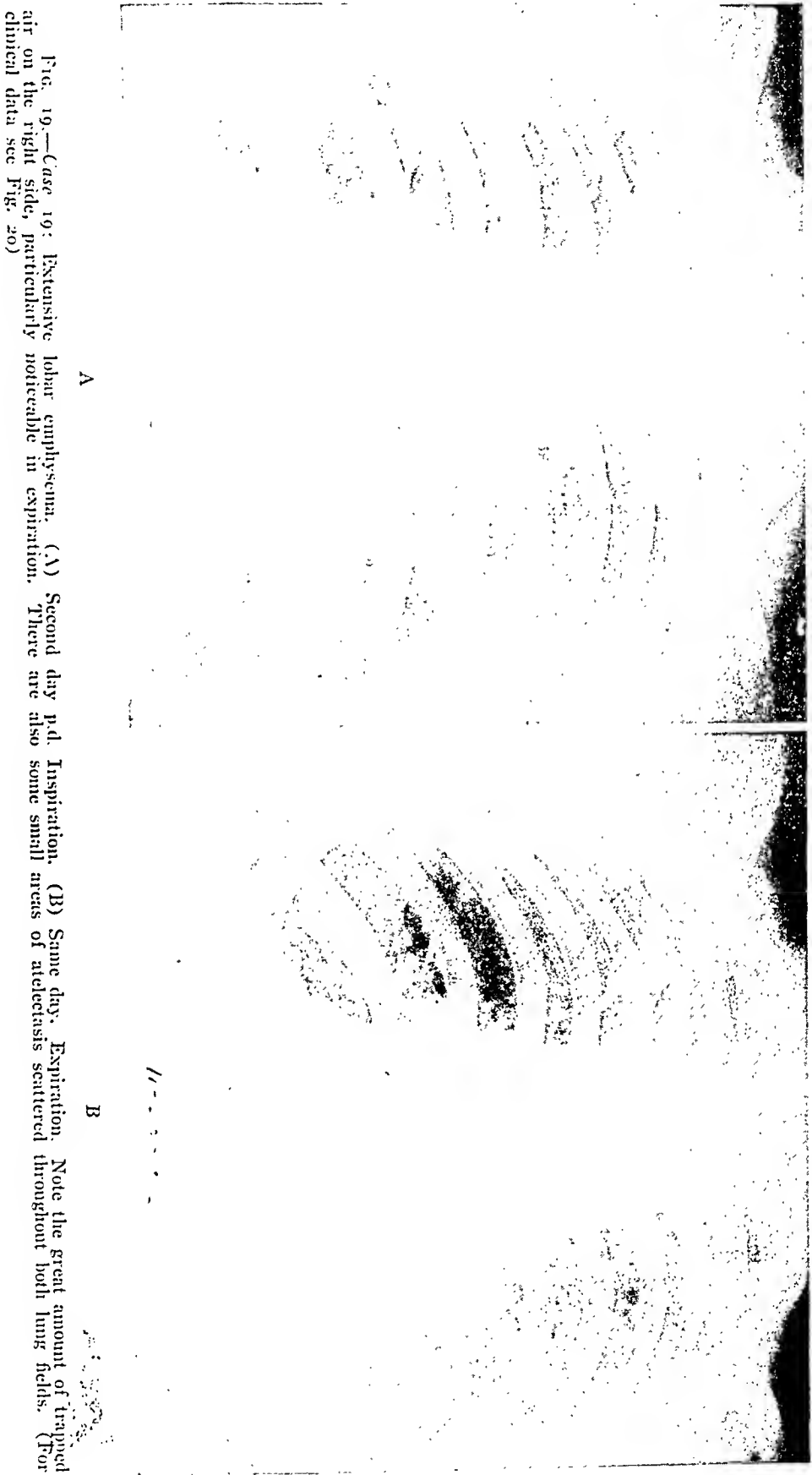
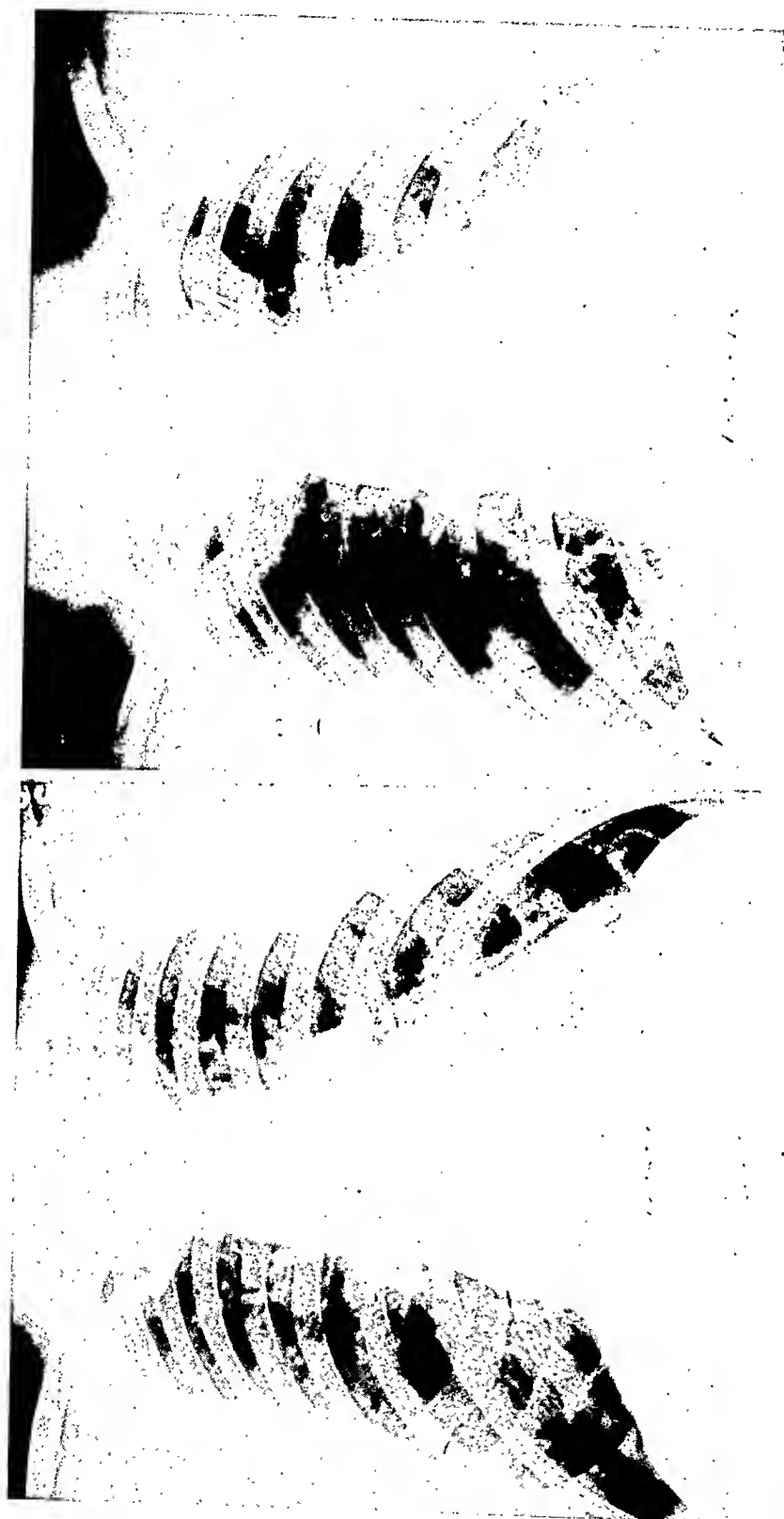


Fig. 19.—Case 19: Extensive lobar emphysema. (A) Second day p.d. Inspiration. (B) Same day. Expiration. Note the great amount of trapped air on the right side, particularly noticeable in expiration. There are also some small areas of atelectasis scattered throughout both lung fields. (For clinical data see Fig. 20)



B

A

FIG. 20.—Case 19 (Continued): Fourth day p.d. (A) Inspiration. (B) Expiration. There is still marked trapping of air on the right side, although less than previously; minimal areas of atelectasis in the left lower lobe.
Clinical Data: Male, age 42. Inhalation burns and moderate burns of head and hand. Many wheezes. On the first day p.d. the patient developed the clinical picture of an asthmatic attack, without preceding history of asthma. Expiratory "push" was absent; markedly diminished vital capacity. The first roentgenologic evidence of trapped air was seen 12 hours p.d. (Not illustrated here). The emphysema improved gradually but there was still some evidence of trapped air on the right side 18 weeks p.d. (See Dr. Aub's report)

X-RAY OF PULMONARY LESIONS

Areas of Emphysema

Several of the patients showed lobular or lobar areas of emphysema during various stages of their pulmonary complication. They were seen best on films in expiration, indicating the presence of trapped air. Areas of atelectasis were usually present simultaneously, while in two cases localized emphysema was the only demonstrable pathology (Cases 15 and 39). Persistent lobar emphysema was the outstanding feature in one of the cases and will be described in detail.

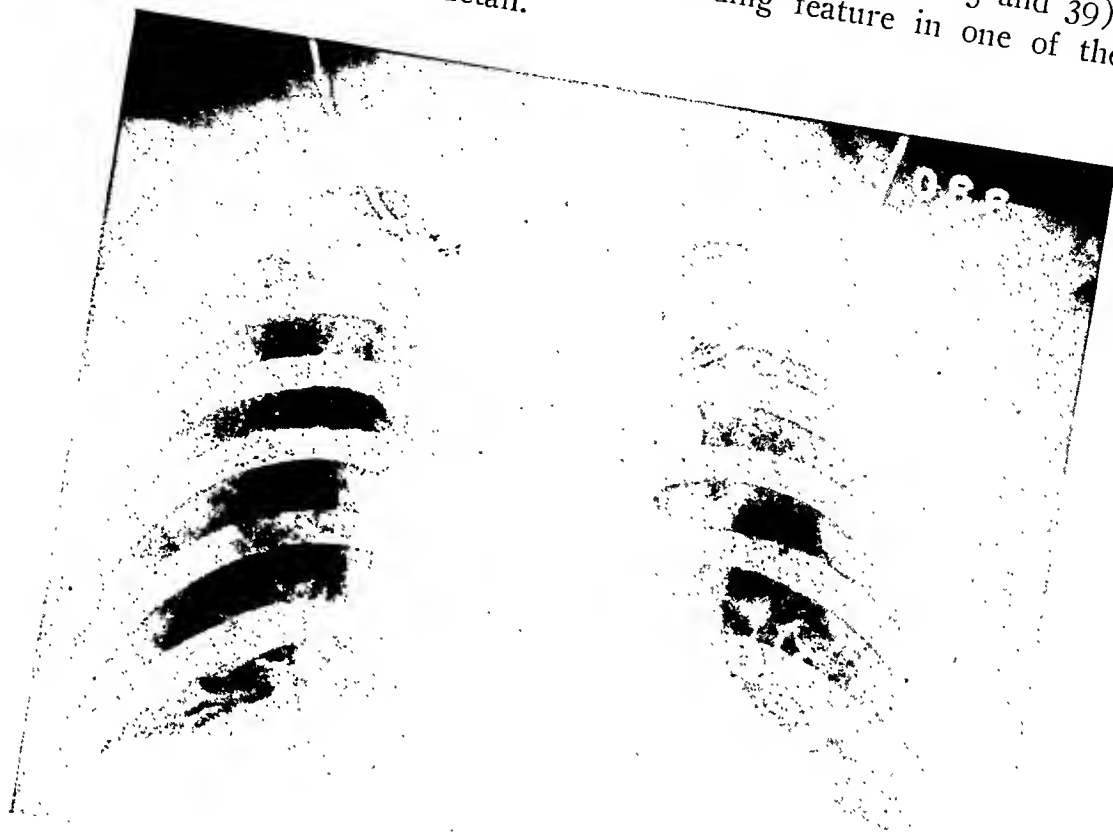


FIG. 21.—Case 26: Fifth day p.d. Plate-like foci of atelectasis in both lung fields, a particularly large one in the left lower lobe. This patient showed no roentgenologic evidence of pathology on the first two days p.d. The first appearance of atelectasis, with some emphysema, occurred on the third day. Four weeks p.d. there was fairly extensive atelectasis in the left lower lobe. Nine weeks p.d. the lungs appeared completely normal.
Clinical Data: Male, age 36. Burns of hands, face and cornea. Lungs were clear on the first day p.d.; coughing continuously on the second day with bubbles at base. Clinically, the lungs cleared up within the first week.

Case 19.—Marked inhalation burns with some additional burns. Râles in both bases, with marked wheeze and tracheal rhonchi noted a few hours p.d. Film taken 12 hours p.d. showed increased brightness in the region of the right lower lobe with some linear areas of atelectasis in this lobe as well as in the left lower lobe and in the bases of both upper lung fields. The right hilus was small. The stomach was dilated and contained a large amount of air. Films taken 30 hours p.d. showed the pulmonary changes more pronounced. Films taken 42 hours p.d. (Fig. 19) revealed the emphysematous changes in the right lung to have increased, and at that time to have involved all of the lobes on the right side with some plate-like areas of atelectasis on this side and larger areas of atelectasis on the left side. There was some mottled increased density in the left upper lobe. The trapped air on the right side was

most clearly visible on the film taken in expiration. The right hilus was small and the right diaphragm was low in position. Daily films were taken up to the eleventh day p.d., and from that time on the examinations were spaced at longer intervals. The areas of atelectasis disappeared gradually and had almost completely gone on the fifth day p.d. The trapping of air in the right lung, however, remained clearly demonstrable, particularly on the films taken in expiration (Fig. 20). Eighteen weeks p.d., the right diaphragm was still slightly lower than the left, and there was still definite evidence of air trapping on the right side. The expiratory "push" in this patient had completely disappeared during the first week p.d. It reappeared gradually, corresponding to the increase in vital capacity which initially had been much below normal.

COMMENT.—The bronchial obstruction in this patient had produced atelectasis in some areas but had caused mainly ball valve obstruction, particularly of the right lung with resulting obstructive emphysema and a clinical picture of status asthmaticus. Air trapping was still present when the patient was seen last (18 weeks p.d.).

Areas of Miliary Mottling

Peculiar mottling was seen in two of the cases (Cases 25 and 33) (Fig. 11). The changes were particularly marked in Case 33. They consisted of diffuse mottling throughout both lungs, a single lesion measuring from about two to six millimeters in diameter. The lesions were fairly well circumscribed but seemed to be confluent in places. There was also some increase in the linear structures of the lung with several characteristic plate-like foci of atelectasis. The mottling in Case 25, much less marked than in the preceding case, was seen only on the postmortem film, and was present only on the right side. Both patients died. Autopsy was obtained in Case 25 (See above). It did not definitely explain the mottling seen in the roentgenogram. The process simulates somewhat the changes described in bronchiolitis obliterans,^{1, 9} although in that disease the single lesions are more discreet and smaller. The mottling in our cases is even more like the miliary lesions seen following inhalation of nitrous gases (Nichols,⁸ Renander¹⁰) and of acid fumes (Doub³). From the combination of linear shadows and fine mottling in the most outspoken of our cases, it is at least possible that the appearance was produced by multiple fine areas of atelectasis, together with the actual demonstration of plugged small bronchi.

Areas of "Drowned" Lung

Early in the process three of the survivors (Cases 2, 20 and 32) showed, in addition to the more characteristic areas of atelectasis, an unusual appearance of the lung field which was not seen in any of the other cases. This process was characterized by an homogeneous groundglass appearance covering the lower half of the left lower lobe in Case 20 (Fig. 17 A), the right upper and middle lung field in Case 2 (Fig. 22 A), and the central portions of both lungs in Case 32 (Fig. 23 B). The lesion was noted in Case 20 on the second and third day p.d., and was no longer present on

X-RAY OF PULMONARY LESIONS



A

B

Fig. 22.—Case 2: (A) Twelve hours p.d. Diffuse haziness in the right upper lobe ("drowned" lung); small areas of atelectasis in the left lower lobe. The pathology in the right lung and behind the heart on the left side. All these lesions had disappeared by the 7th week p.d. Plate-like foci of atelectasis in the medial aspect of the left leg veins. The lungs, however, appeared otherwise normal.

Clinical Data: Female, age 38. Extensive inhalation burns in addition to other burns. Great respiratory difficulty. Patient was fibrillating for several hours following admission to the hospital. Later the heart appeared normal. Patient developed clinical and roentgenologic evidence of pulmonary infarcts in the 7th week p.d., apparently due to thrombophlebitis of the left leg veins. The lungs, however, appeared otherwise normal.

the fourth day. It was seen on the first day p.d. in Case 2, and had disappeared on the second day p.d. In Case 32 it did not appear before the second day, decreased on the fourth day, was still somewhat visible on the sixth day, but had disappeared on the seventh day. In contradistinction to large areas of atelectasis there was no evidence of decrease in the size of the involved portions of lung. In Cases 20 and 2 the lesion occurred too early and disappeared too rapidly for pneumonia; whereas it is not possible to rule out pneumonia in Case 32. The appearance was similar to that occasionally seen in asymmetrical pulmonary edema in patients with nephritis or heart failure. Considering the course of the lesions, however, the pathology can best be explained by the accumulation of fluid in the alveoli distal to points of bronchial obstruction. The pathologist Loeschcke⁷ describes partial displacement of air by fluid in atelectatic portions of the lung, and the "drowned" lung distal to areas of bronchial obstruction (foreign body, tumor) is a well known clinical occurrence.^{2, 6} Fluid was actually found in the alveoli of some of the atelectatic areas in our autopsied cases. (See Dr. Mallory's report.) The fact that atelectasis occurred later in the originally "drowned" area in Case 20 further supports the validity of the suggested mechanism.

Pulmonary Edema

Pulmonary edema was extensive only in the two victims who were dead on arrival. As discussed before the origin of this pulmonary edema is not known. It may have been caused by carbon monoxide poisoning. In any case, it seems unlikely that it was caused by the same mechanism which produced the pulmonary changes found in the two survivors. One of the patients (Case 7) who died two days p.d. developed pulmonary edema shortly before death, but this terminal pulmonary edema was probably not related to the characteristic pulmonary damage produced by the catastrophe. Aside from this case, pulmonary edema was not seen in any of the survivors, although the question of atypical asymmetrical pulmonary edema arose in three patients. (See paragraph on "Drowned" lung.)

Infarcts

Infarcts were not diagnosed roentgenologically in the first few days following the catastrophe. Two of the autopsied cases (Cases 7 and 27) showed areas in which the alveoli were slightly decreased in size and contained blood but no air. The cell walls were preserved. These lesions were thought to be areas of early infarction, possibly superimposed on areas of atelectasis. (See Dr. Mallory's report.) It is possible that changes which roentgenologically were interpreted as plate-like areas of atelectasis in some of the survivors actually represented small infarcts. It is unlikely, however, that many infarcts were misinterpreted in this manner, inasmuch as the roentgenologic evidence of the lesion commonly changed back-and-forth from day to day, which would not occur in infarcts. Furthermore,

X-RAY OF PULMONARY LESIONS



Fig. 23.—Case 32: (A) Twelve hours p.d. Extensive areas of atelectasis behind the heart on the left side as well as in a patchy manner in both upper lung fields. The next day the atelectasis had improved. There were beginning changes in both middle lung fields, more marked on the 3rd day. (B) Third day p.d. Extensive pathology in both middle lung fields, the nature of which is not definitely established—"drowned" lung; atelectasis, or pneumonia. This process disappeared by the 7th day p.d. but small areas of atelectasis were still visible in the 4th week. The lungs appeared normal in the 7th week p.d. (Fig. 24).

all the lesions disappeared without leaving any trace of a scar with the exception of one patient (Case 13). Areas of incomplete infarction may clear up without visible scar,⁴ but it is not probable that so few scars would result if an appreciable number of infarcts had been present among the survivors. Infarcts did occur, and were seen roentgenologically in some of the severely burned cases several weeks following the disaster, obviously connected with thrombophlebitis.

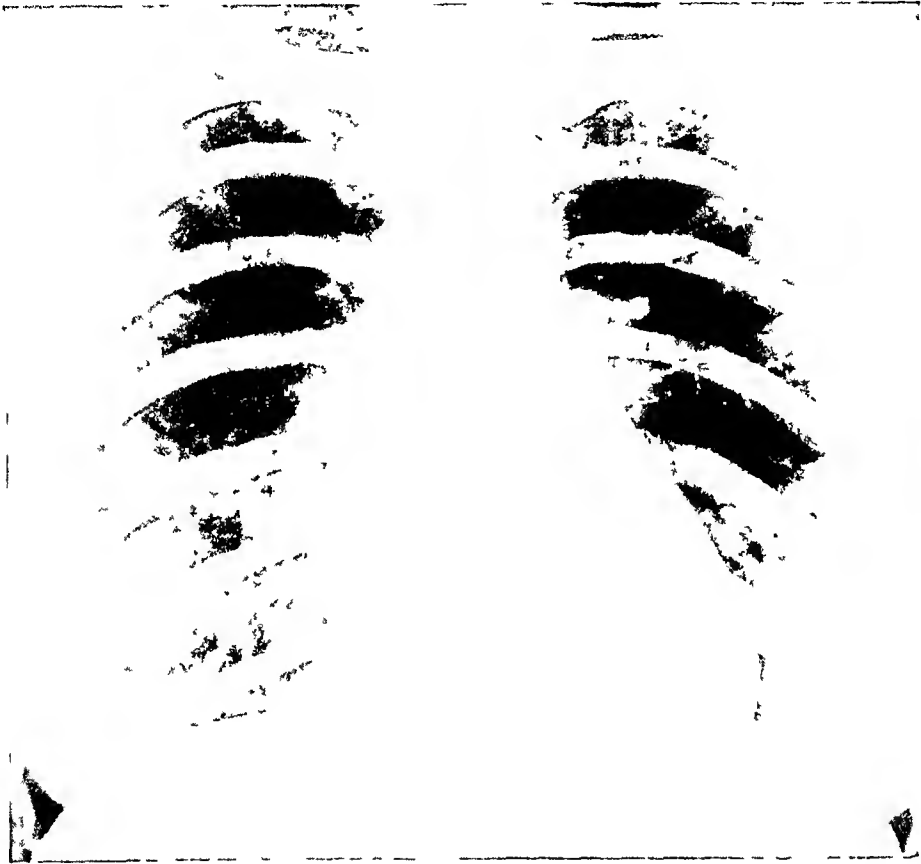


FIG. 24—Case 32 (Continued). Normal lung in the 7th week p.d.
Clinical Data Female age 35 Burns of lips, nose and tongue, moderate burns of forehead and hands Unconscious, severe cerebral complications (See Dr Cobb's report for further details)

Acute Dilatation of the Stomach

Marked dilatation of the stomach was seen on the chest films in five cases (Cases 2, 19, 27, 33 and 34). In Case 27, the esophagus was also markedly dilated and air-filled (Fig. 10 A). Three of these patients died. It is possible that the dilatation was a sign of general shock although the exact relationship remains obscure.

Follow-up of the Pulmonary Lesions

Most of the patients were examined repeatedly, regardless of whether or not the lungs appeared normal roentgenologically. These follow-up exam-

X-RAY OF PULMONARY LESIONS

inations were continued until finally the roentgenographic appearance of the lungs was normal in all but two cases. One patient showed evidence of persistent air-trapping at the end of 18 weeks (Case 19), while another still had a linear area of atelectasis in the 17th week (Case 13).

PATIENTS SHOWING NO ROENTGENOLOGIC PULMONARY CHANGES

Thirteen patients admitted to the ward showed no roentgenologic pulmonary changes. One of them (Case 12) died 27 hours p.d., with clinical signs of respiratory embarrassment. These signs developed, however, some hours after the negative film had been obtained.

All but two of the surviving roentgenologically-negative patients presented râles on physical examination on one or several occasions as evidence of some bronchial involvement. In spite of this, the roentgenologic examination of the chest failed to show any evidence of pathology. It is likely that the bronchial lesions in these cases were of a minor degree and had not led to interference with the aeration of the lungs.

DISCUSSION

This report shows that the abnormal roentgenologic appearance of the lungs in the survivors of the Cocoanut Grove disaster was caused primarily by damage to the bronchi and bronchioles. The roentgenologic changes may be characterized as a classical example of diffuse damage to these parts of the upper respiratory tract. Similar roentgenologic appearances may result from many other causes of widespread bronchial injury, and in the recognition of this fact lies the importance of this experience in a broader sense. In infants with bronchiolitis and peribronchiolitis, the roentgenograms show areas of atelectasis and emphysema like those described in this report. Damage to bronchioles scattered throughout the lungs from various gases or from inhalation of food or water may produce similar pathology and similar roentgenologic findings. During war-time such trauma is likely to be a frequent occurrence, and early recognition of the mechanism involved will be of value in the determination of the correct treatment.

SUMMARY

1. Thirty-five of the survivors of the Cocoanut Grove disaster were examined roentgenologically following their admittance to the hospital. Pulmonary pathology was found at some time in 22 patients, whereas the examination of the other 13 was negative at all times.
 2. The roentgenologic appearance of the lungs was bizarre and varied from patient to patient. The majority of the lesions, however, could be explained by areas of atelectasis and emphysema, both apparently due to bronchial occlusion, particularly of the smaller branchi.
- Atypical lesions (miliary nodules, and areas of "drowned" lung) were seen in a few cases.

Diffuse pulmonary edema was found in two victims who were dead on arrival.

Infarcts were not recognized roentgenologically in the first period following the fire, although some may have existed.

3. Acute dilatation of the stomach was found in five patients; and of the esophagus in one patient.

4. The follow-up of the pulmonary lesions is described. The lesions of all the survivors finally disappeared except in two cases.

5. The experience gained from this disaster is of value as it applies to the recognition of the roentgenologic appearance of lungs in cases with damage to the bronchi and bronchioles from other causes.

REFERENCES

- ¹ Assman, H.: *Klinische Röntgendiagnostik der inneren Erkrankungen*, Leipzig, 1929.
- ² Bowen, D. R.: Acute Massive Collapse of the Lung. *Am. J. Roentgen*, **21**, 101-141, 1929.
- ³ Doub, H. P.: Pulmonary Changes from Inhalation of Noxious Gases. *Radiology*, **21**, 105-113, 1933.
- ⁴ Hampton, A. O., and Castleman, B.: Correlation of Postmortem Chest Teleroentgenograms with Autopsy Findings: With Special Reference to Pulmonary Embolism and Infarction. *Am. J. Roentgen.*, **43**, 305-326, 1940.
- ⁵ Fleischner, F., Hampton, A. O., and Castleman, B.: Linear Shadows in the Lung. *Am. J. Roentgen.*, **46**, 610-618, 1941.
- ⁶ Jackson, C.: The Drowning of the Patient in his Own Secretion (editorial). *Laryngoscope*, **21**, 1183-1185, 1911.
- ⁷ Loeschke, H.: Störungen des Luftgehalts (in Henke-Lubarsch *Handbuch d. speziellen pathologischen Anatomie und Histologie*, Vol. 3, 1st part, Berlin, 1928).
- ⁸ Nichols, B. H.: The Clinical Effects of the Inhalation of Nitrogen Dioxide. *Am. J. Roentgen.*, **23**, 516-520, 1930.
- ⁹ Rabin, C. B.: Radiology of the Chest (in Nelson's *Diagnostic Roentgenology*, edited by R. Golden, Vol. I, p. 196-Z, 1941).
- ¹⁰ Renander, A.: Röntgenologisch beobachtete reversible Veränderungen bei nitrosen Gasschaden an den Lungen. *Acta Rad.*, **17**, 152-159, 1936.
- ¹¹ Volhard, F.: Personal communication.

PATHOLOGY: WITH SPECIAL REFERENCE TO THE PULMONARY LESIONS

TRACY B. MALLORY, M.D., AND WILLIAM J. BRICKLEY, M.D.

DEPARTMENT OF PATHOLOGY AND BACTERIOLOGY, MASSACHUSETTS GENERAL HOSPITAL, AND THE OFFICE OF THE
MEDICAL EXAMINER FOR SUFFOLK COUNTY, NORTHERN DIVISION, BOSTON, MASSACHUSETTS

SIX POSTMORTEM EXAMINATIONS were performed either at the Northern Mortuary of Suffolk County or in the Pathology Laboratory at the Massachusetts General Hospital. Although these represent a very small percentage of the victims of the holocaust, the findings parallel so closely in most respects the results of some 16 other autopsies performed elsewhere in the city that they may be considered fairly representative. Material for histologic examination from five other cases was also made available to us but provided so little additional information that its formal presentation seems unnecessary. The six cases examined by us personally fell into two groups: Three cases which were dead on arrival; and three which died after varying, but comparatively brief (40-62 hours) periods of treatment upon the wards.

It was apparent from inspection of the bodies which were delivered to the hospital and to the mortuary that only a small proportion of the victims had suffered extensive enough surface burns to account for death and that a search for contributory factors was in order. The most obvious of these was carbon monoxide poisoning, which was apparent clinically, and was confirmed at autopsy, by the finding of 42 per cent and 50 per cent saturation of the hemoglobin in samples obtained from the right heart in two cases dead on arrival. Although significant as a contributing factor this degree of monoxide saturation could not in itself be considered lethal. In one case a sample of gas collected by suction from the respiratory tract showed on chemical examination traces of oxides of nitrogen with a test sensitive to 50 parts per million. Since a second sample was negative the results must be regarded as equivocal. Beyond this point postmortem studies were entirely in accord with early clinical impressions in emphasizing the great importance of the involvement of the respiratory tract. The bulk of this report will, therefore, be devoted to the findings in the upper respiratory tract and in the lungs.

CASES DEAD ON ARRIVAL

The three cases which were dead on arrival presented lesions so similar that only one needs to be recorded. An abbreviated protocol follows:

Protocol.—The body is that of a well-developed and well-nourished young woman, estimated to be about age 25. It shows severe second and third degree burns of the head, face, neck, both arms, the chest above the breasts and the entire back to the level of the sacrum, including essentially all skin areas which would be exposed by a conventional evening gown cut relatively low in front and to the gluteal fold behind. Scattered first and second degree burns with extensive vesiculation are present on the legs, particularly the medial surfaces above and below the knees. The entire face and the neck have an edematous, bloated appearance.

With the initial incisions it is apparent that the muscles and most of the internal organs are a brilliant cherry-red in color. This is not apparent in the blood that escapes from severed vessels or in the chambers of the heart which appears dark red. A sample of this blood, however, submitted for chemical analysis showed 42 per cent saturation with carbon monoxide.

The trachea and larger bronchi contain considerable amounts of partially digested food similar in character to that which is present in the stomach. The underlying mucosa is diffusely reddened and shows numerous pin-point hemorrhages which are most frequent in the upper trachea and decrease as one descends the bronchial tree but scattered foci can still be found in bronchi 3 mm. in diameter. No exudate is present and no froth.

The lungs weigh 1230 Gm. together. They are bright pink, heavy, voluminous, and do not collapse (colored section Fig. 1). Crepitation is uniformly diminished but nowhere entirely absent. Fragments of the tissue float in water. The pleura is smooth, glistening and transparent, the underlying parenchyma brilliant pink in color. Several subpleural hemorrhages 5 to 10 mm. in diameter are found over the lower lobes. On section, all lobes present uniform, congested but very bright red surfaces. On slight pressure considerable quantities of blood-stained fluid ooze from the freshly cut surfaces but this is not frothy. The pulmonary arteries and veins are normal.

The heart, liver, kidneys, spleen and internal genitalia are normal except for cherry-red discoloration of all blood containing areas. The gastro-intestinal tract is normal except for congestion and petechial hemorrhage throughout the duodenum. The brain shows only an unusual pinkish tinge to the grey matter.

Microscopic Examination: The trachea and primary bronchi show essentially similar changes (Fig. 25). All vessels internal to the cartilaginous ring are maximally dilated. The areolar tissue of the mucosa is markedly edematous and at intervals of 2 to 3 mm. shows focal hemorrhages 0.5 to 1.0 mm. in diameter. Almost no leukocytes are found outside of vascular lumina. The basement membrane is normal and the majority of the epithelial cells have desquamated. No ciliated or goblet cells persist but a single layer of small cells with scanty undifferentiated cytoplasm adheres to the basement membrane in many places. No coagulation necrosis or eschar formation can be made out.

Several sections from various portions of the lungs present essentially similar pictures. The great majority of the alveoli are of normal or slightly subnormal size and are filled with precipitated eosinophilic material, partly granular and partly homogeneous. In the latter instance it occasionally reaches almost the density of thyroid colloid (Fig. 26). In some alveoli considerable numbers of red blood cells are present and these are almost invariably found in association with the homogeneous rather than the granular precipitate. Scattered between these edematous alveoli are bubbles of air ranging from two to three times the size of the alveoli. These are invariably localized in dilated atria and respiratory bronchioles and do not represent emphysematous alveoli (Fig. 27). There is, thus, very little intermingling of air and fluid. The capillaries of the alveolar walls and all small blood vessels throughout the lungs are congested. The interlobular septa are widened and edematous, and the lymphatics here and in the perivascular tissues are frequently dilated and contain granular precipitate. The small bronchi show desquamation of epithelium and no necrosis or inflammatory reaction. Nowhere in the sections is there leukocytic infiltration. Several bronchioles and a few alveoli contain aspirated vegetable cells.

Microscopic examination of sections of other organs show no significant variations from normal. The liver cells present the granular, dispersed cytoplasm and prominent cell membranes characteristically seen in cases of sudden death in the glycogen-storage phase of metabolic activity.

The major parenchymal lesion in this case, as well as in the others of

PATHOLOGY OF THE RESPIRATORY TRACT

FIG. 25.—Trachea from case dead on arrival. The epithelium is desquamated, the mucosa edematous without leukocytic infiltration. A focus of hemorrhage is present in the superficial portion. The mucosal blood vessels are maximally dilated.



FIG. 26.—Lung of the same case demonstrating massive pulmonary edema with bubbles of trapped air.

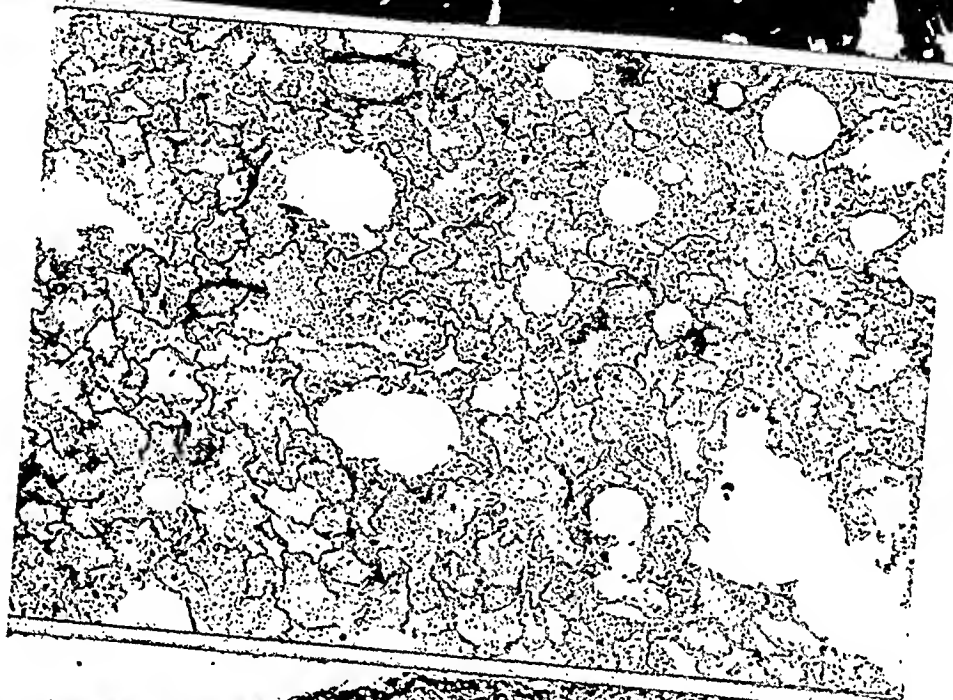
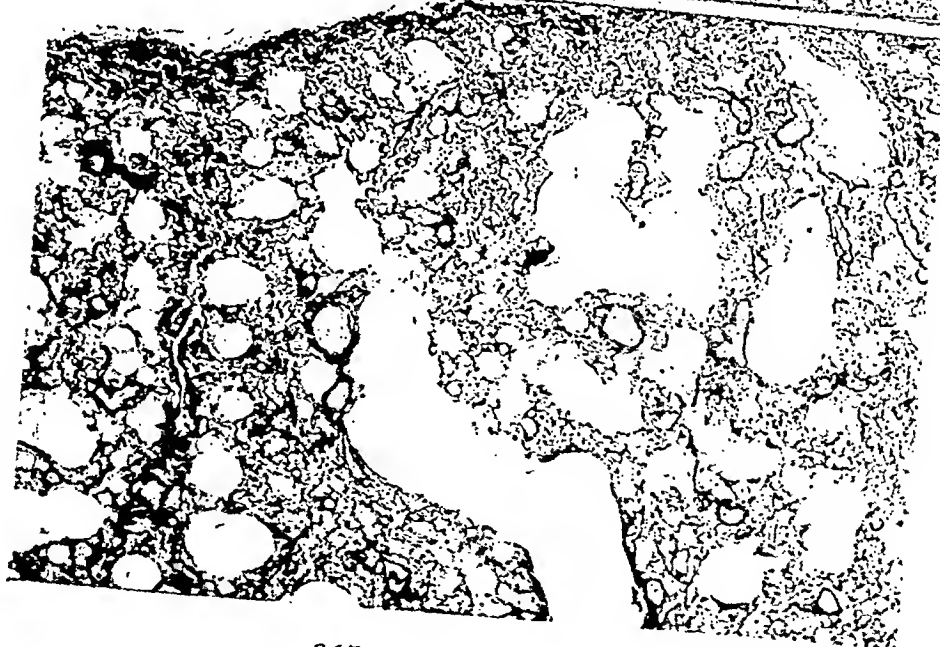


FIG. 27.—Another area demonstrating that the trapped air lies predominantly in dilated respiratory bronchioles and atria rather than in emphysematous alveoli.



the group dead on arrival, was the diffuse pulmonary edema. A slightly unusual feature was the absence of froth in the trachea and bronchi as well as in the fluid which oozed from the cut surfaces. This appeared to be explained by the fairly sharp limitation of the edema to the alveoli themselves. Such air as was present was found in atria and respiratory bronchioles. There was, consequently, comparatively little actual admixture of air and fluid. A high protein content of the edema fluid was evidenced by the homogeneous colloid-like precipitation in the alveolar lumina, and the presence of red blood cells confirmed the existence of significant capillary damage.

These cases were too long postmortem (36 hours) to attribute safely significance to the desquamation of the tracheal and bronchial epithelium. The absence of any eschar formation and the intact basement membrane, however, make it doubtful, in these cases at least, that flames could have been inhaled far into the respiratory passages. That some physically or chemically irritating agent was so inhaled is indicated by the vascular dilatation, the marked edema of the tracheal and bronchial mucosae and the presence of innumerable pin-point hemorrhages. It seems probable that the pulmonary edema was of similar pathogenesis. The aspiration of vomitus was not responsible since similar changes were found in other cases in which no evidence of such aspiration was present.

CASES TREATED IN THE HOSPITAL

Three cases came to autopsy from the group which were admitted to the ward. Case 25 died 40 hours, Case 7, 52 hours, and Case 27, 62 hours after admission. They will be presented in that order:

Case 25.—The body is that of a powerfully built, large man, age 46. The hair has been extensively singed but the scalp is free from discoloration or vesiculation. There are first, second and third degree burns covering the entire face and upper neck, the areas of third degree burn being comparatively small and localized about the mouth, nose, chin and ears. The mucous membrane of the lips is blistered. The hairs of the nostril are singed, and greyish adherent exudate is visible in the nostrils and overlying the inferior turbinates. The entire face is swollen and edematous, especially the periorbital tissues. The conjunctivae are congested but the sclerae are intact. First, second and third degree burns are likewise found on both hands, particularly on the dorsal surfaces, where they extend up to the cuff line.

Respiratory Tract: The larynx when viewed from above appears completely occluded by edematous swelling of the mucous membranes, particularly those overlying the false cords and the aryepiglottidean folds. Fibrinopurulent exudate overlies the former. The surfaces are glazed and whitish in color but there is no ulceration or membrane formation (color section Fig. 3). When the larynx is viewed from below (color section Fig. 4), in contrast, a greenish-black membrane, to which black fragments of charred material are adherent, extends from the inferior surface of the true cords downward, encircling the trachea for a distance of 2.5 cm. The membrane can be stripped from the mucosa only with difficulty and leaves a raw, hemorrhagic surface. The mucous membrane of the remainder of the trachea is intensely red with scattered petechial hemorrhages. Foci of ulceration and membranous exudation are absent for a distance of 4 cm. below the zone described above, then begin again as scattered foci 2 to 10 mm. in diameter in the middle and lower thirds of the trachea, and become almost confluent again in the primary bronchi.

PATHOLOGY OF THE RESPIRATORY TRACT

The lungs are extremely voluminous and fail to collapse on removal of the sternum. They are heavy, of diffusely increased consistency, and are subcrepitant throughout. Along the margins of all lobes, however, is a zone 2 cm. in width which is lighter in color, and more normal in consistency than the central parts of the lung (color section Fig. 2). Air is evidently trapped in this peripheral zone since it fails to collapse even after removal from the thorax. Several emphysematous blebs are evident at each apex.

The left lung is sectioned at once, the right one saved for lipiodol injection, roentgenologic examination, and fixation before sectioning. On opening the bronchial tree all bronchi down to 3 mm. in diameter show intensely red, hemorrhagic mucosae overlaid by a greenish fibrinous membrane (color section Fig. 6). This is in places rather firmly adherent, in other areas strips readily and in still other places has spontaneously desquamated into the lumen to form occlusive bronchial casts. The lung parenchyma in the central two-thirds of each lobe is deep red in color and moderate amounts of pinkish fluid can be expressed by gentle pressure. A zone averaging 2 to 3 cm. at the periphery of the upper and middle lobes and 1.5 cm. in the lower lobe is paler and comparatively well aerated. Section of the left lung, fixed by instillation of formalin into the bronchial tree, shows similar hemorrhagic, membranous bronchitis throughout the major radicles of the bronchial tree. In addition, it shows extensive anatomic emphysema of the upper anterior half of the upper lobe. Through this area the alveoli average 2 to 3 mm. in diameter and numerous bullae 5 to 10 mm. in diameter are present. Minor focal spots of emphysema 2 to 3 mm. in diameter associated with dense anthracotic deposits are scattered throughout the remainder of the upper lobe and also are present in the lower lobe. Slight atheromatous deposits are present in the major pulmonary arteries. The remainder of the autopsy shows moderate cardiac hypertrophy without valvular lesions; slight coronary sclerosis without narrowing of the lumina; moderate atherosclerosis of the aorta; a large, deeply congested but evidently fatty liver; congested kidneys from which the capsules strip with slight difficulty leaving slightly granular surfaces; a fatty pancreas and a right inguinal hernia.

Microscopic Examination: Larynx, Trachea and Primary Bronchi: These show similar pictures, varying, however, from one area to another in the intensity of the reaction. All sections show complete desquamation of the epithelium except in pockets about the mouths of the gland ducts. The basement membrane is in most areas intact. In one section it and the underlying 30 to 40 microns of tissue are necrotic. In another section, evidently from near the larynx, epithelium and basement membrane are missing and have been replaced by a diphtheritic membrane consisting of sheets of parallel fibrinous lamellae with polymorphonuclear leukocytes between the lamellae. In all sections the small vessels are maximally engorged, and there is edema and polymorphonuclear infiltration of the submucosa. In many sections there is, likewise, evidence of a chronic inflammatory process shown most clearly by foci of fairly dense lymphocytic infiltration in the stroma of the mucous glands.

Lower Bronchial Tree: The findings vary considerably in different bronchi and bronchioles, apparently independently of their size. None are normal, since vascular engorgement and polymorphonuclear infiltration are invariable. In some bronchi the epithelium has partially or completely desquamated and masses of detached but fairly normal looking ciliated and goblet cells are found in the lumina intermixed with mucin and polymorphonuclear leukocytes. In other bronchi the cells may stain normally but show a tendency to separation by edema fluid and leukocytic infiltration. In other places the basement membrane. In these cases the cells have partially or completely lost the tendency to separation by edema fluid and their nuclei have partially or completely lost the power of retaining the stain. These necrotic epithelial cells are found singly and but are completely acidophilic and their nuclei have partially or completely lost the power of retaining the stain. These necrotic epithelial cells are found singly and in clumps in the bronchial lumina where they are combined with leukocytes, mucin

and fibrin to form occlusive bronchial plugs (Fig. 28). In one bronchus the mechanism of detachment of the necrotic epithelial cells is clearly shown by the presence of vesicles filled with clear fluid and a few leukocytes between the necrotic cells and the basement membrane. Only rarely is there evidence that the basement membrane itself has been destroyed. In these areas a typical diphtheritic membrane similar to that noted in the upper trachea is present. In many bronchi evidence of a preexisting chronic inflammatory process is present in the form of lymphocytic infiltration of the mucosa and mucous glands.

Lungs: The pulmonary parenchyma proper shows an alternation of partially collapsed air sacs which often contain precipitated edema fluid and overdistended air passages containing trapped bubbles of air. The majority of the air-filled structures can be identified as respiratory bronchioles and atria rather than alveoli. The presence, however, of true anatomic emphysema, bordered by foci of fibrosis and either anthracosis or lymphocytic infiltration makes the distinction between anatomic and physiologic emphysema very difficult. Both are certainly present but their relative proportions cannot be judged with accuracy.

The edema fluid in the alveoli is demonstrated in part by granular, in part by homogeneous precipitate. It is assumed that the latter indicates a higher protein content. There is minimal extravasation of erythrocytes. An occasional lobule shows frank pneumonic exudate with many polymorphonuclears, some monocytes and but little fibrin. In these areas colonies of micrococci are present and a few cocci can be identified in the cytoplasm of the polymorphonuclears.

Liver: Occasional cells are coarsely and nearly all cells finely vacuolated with fat. The space between the liver cords and the sinusoidal endothelium is almost uniformly widened, a finding usually considered indicative of hepatic edema.

Pancreas: Negative except for the presence of considerable amounts of adipose tissue.

Kidney: The intima of the intermediate-sized and larger arteries is thickened with considerable reduplication of the elastic lamellae. Small foci of atrophic tubules and an occasional sclerosed glomerulus are seen. A few tubules contain bluish-staining hyaline casts.

On opening the head, very marked edema of the deep areolar tissues of the scalp is noted. The brain is normal except for congestion of the meningeal vessels and edema of the arachnoid.

In summary, a forty-six-year-old man, of powerful physique, showed evidence of long-standing chronic bronchitis, moderately severe pulmonary emphysema, slight pulmonary and moderate systemic arteriosclerosis, fat infiltration of the liver and pancreas, slight hypertrophy of the heart and mild nephrosclerosis. Upon these chronic lesions were superimposed severe but not extensive cutaneous burns of the head, neck and hands. The outstanding lesions were a necrotizing membranous inflammatory process in the upper respiratory tract which produced almost complete laryngeal stenosis, and a similar process in the intrapulmonary bronchial tree resulting in diffuse bronchostenosis. Though tracheotomy would have relieved the laryngeal stenosis, the degree of bronchial obstruction was so great that no air-way could have been established. The pulmonary parenchyma, already handicapped by extensive pulmonary emphysema, was drowned by massive pulmonary edema. Only at the periphery of the lung were there narrow aerated zones in which air had evidently been trapped by the diffuse bronchostenosis. Gross atelectasis was absent.

PATHOLOGY OF THE RESPIRATORY TRACT

Case 7.—The positive findings of the autopsy are as follows: The body is that of a powerfully built, well-nourished male, age 29. Almost the entire face, the scalp and the posterior portion of the neck are covered by first and second degree burns. These are particularly severe and reach third degree in the region of the alae nasi and the margins of the ears. The posterior surface of both hands and wrists running up 3 cm. above the ulnar styloid show third degree burns. Burns are also present on both ankles just above the shoe level. There is a recent tracheotomy incision 5 cm. in length, the central portion of which is gaping and from which the tracheotomy tube has been removed. Hematomata are present in both antecubital fossae as well as the scars of several needle punctures overlying the veins. The subcutaneous fat is abundant. The muscles are well developed, normal in color and consistency.

Stomach: Contains approximately 300 cc. of greenish-brown fluid. The mucosa shows innumerable red puncta varying from 0.5 to 2 mm. in size. These are most numerous at the cardiac end and disappear as the pyloric antrum is reached. No true erosions are found.

Duodenum: There is moderate congestion and numerous scattered minute petechiae in the mucosa of the second and third portion. The remainder of the intestinal tract is negative.

Larynx and Trachea (color section Fig. 5): All mucous membranes in the larynx are markedly congested and swollen, producing almost total occlusion at the level of the true cord. Over the arytenoid cartilages the mucous membrane is 3 to 4 mm. thick. Lightly adherent to the mucous surfaces are grayish spots of fibrinous exudate in which are small, black charred particles. On the edges of the fibrinous membrane, focal hemorrhage can easily be made out. The hemorrhage and discoloration are present in the larynx below the vocal cords as well as above them. As one passes down the trachea intense hemorrhagic congestion continues but the fibrinous membranes disappear except for scattered linear erosions 2 to 4 mm. in length and 1 to 1.5 mm. in width. The tracheotomy wound is clean and shows no evidence of infection. All the tissues of the lower neck are markedly edematous and this edema spreads downward over the anterior chest wall beneath the pectoral muscle, and also down into the anterior mediastinum in the region of the thymus.

Lungs: Combined weight 1630 Gm. When examined *in situ* it is evident that they collapse only slightly on removal of the sternum. The anterior margins of both upper lobes which present through the sternotomy incision are light in color and the borders are rounded. Alveoli are clearly visible to the naked eye, indicating physiologic emphysema. The major portions of both upper lobes and of the middle lobe are dark pink with a slight violaceous tinge. The tissue feels heavy and is of increased consistency but, nevertheless, still crepitant. No areas of true consolidation can be felt. Two-thirds of the left lower lobe is similar in consistency whereas the posterior inferior third is completely atelectatic and dark reddish-blue and moderately firm. The right lower lobe is likewise heavy, with diffusely decreased crepitation except for a transverse band of complete atelectasis 5 cm. in width, the lower border of which lies 4 cm. above the diaphragmatic margin. Section of the unfixed right lung demonstrates extensive membranous bronchitis extending even to the bronchioles which are dilated and can be traced to within 0.5 cm. of the pleural surface. The membrane is less adherent than in Case 25, is more mucoid and more often stained by hemorrhage. The cut surface of the lung is deeply congested, slightly firmer than normal and diffusely subcrepitant. Moderate amounts of fluid can be expressed with pressure. In the middle third of the lower lobe it is completely atelectatic, very dark red and moderately firm. Several small, frankly hemorrhagic foci, usually lobular in dimensions, are found in contact with pleural surfaces. These suggest infarction but are less firm than would be expected.

Section of the left lung after fixation shows a uniform reddish-chocolate color, alveoli which are just visible to the naked eye and no variations in consistency. The lower lobe in contrast shows marked variations. An irregularly pyramidal area, with a base 4 cm. in diameter along the diaphragmatic surface, extends upward in a zig-zag pattern along the posterior surface of the lobe for a distance of 11 cm. It is dark red in color and depressed 2 to 3 mm. below the adjoining parenchyma. In the fixed specimen it is extremely firm. The cut surface is, likewise, dark red in color, frankly hemorrhagic and completely homogeneous. No air bubbles are present and no trace of alveolar markings can be discerned. At its upper margins the hemorrhagic process sends finger-like processes toward the hilus which are localized in the adventitia of large vessels and bronchi. The configuration of the lesion is very characteristic of atelectasis but its consistency and appearance on section is that of infarction. The remainder of the lower lobe shows compensatory physiologic emphysema, the alveoli averaging nearly twice the size of those in the upper lobe.

Mediastinum: The tissues of the anterior mediastinum are distinctly congested and edematous. As mentioned above this appears to be a dependent drainage of fluid from the more massive edema in the lower neck.

Liver: Weight, 2265 Gm. It seems large even in proportion to the patient's size. It is, in general, deep reddish-brown with some focal yellowish mottling. On section, the markings are not prominent, and the tissue does not pout over the cut edge.

Spleen: Weight, 260 Gm. It is very firm, intensely congested. Considerable pulp scrapes readily from the cut surface. The markings are not evident.

Adrenals: Normal.

Kidneys: Weight, 370 Gm. They are intensely congested. The capsules strip readily leaving a smooth surface. The cortex averages 6 mm. in thickness. The pelves show scattered minute petechial hemorrhages.

Microscopic Examination.—*Larynx and Trachea:* The simplest change is a loss of the lining epithelial cells which have been replaced by a fibrinous membrane of varying thickness in which black granules, presumably carbonaceous, are embedded. This fibrinous layer appears loosely adherent and has frequently been detached in the process of sectioning. Beneath these areas the basement membrane is intact, the underlying areolar tissue is edematous but contains no fibrin deposit and comparatively little leukocytic infiltration. Where epithelium persists it is represented by a narrow layer, one or two cells thick, of spindle-shaped basophilic cells, the long axes of which parallel the basement membrane. Though no mitoses are found one may legitimately surmise early regeneration.

In the more severely involved areas a different picture is observed (Fig. 29). The mucosal surface is lined by a necrotic layer in which two zones can usually be recognized. Toward the lumen is a hyaline, brightly acidophilic, sometimes "fibrinoid" zone 50 to 100 microns in thickness, which is usually devoid of any recognizable structural pattern and is cell free except for small numbers of infiltrating leukocytes. In a few areas, however, shadow forms of the original cylindrical ciliated cells can be recognized within it, suggesting that, in part at least, this hyaline zone has formed by necrosis and fusion of the epithelial layer. Beneath this hyaline zone is another zone, 100 to 200 microns in thickness, of true fibrin deposit and dense leukocytic infiltration. This zone appears to lie just beneath the basement membrane, wherever remnants of it can be identified.

All the blood vessels of the mucosa appear maximally dilated and engorged. A number of the superficial vessels close to the fibrinous layer just described contain thrombi which partially or totally occlude the lumina. In the smaller vessels closest to the surface these thrombi are often dense and hyaline; in the larger ones they are of ordinary platelet and fibrin structure. The loose connective tissue of the deeper portions

PATHOLOGY OF THE RESPIRATORY TRACT

FIG. 28.—Small bronchus from Case 25 completely occluded by a plug made up of desquamated necrotic epithelium, leukocytes, fibrin and mucin.

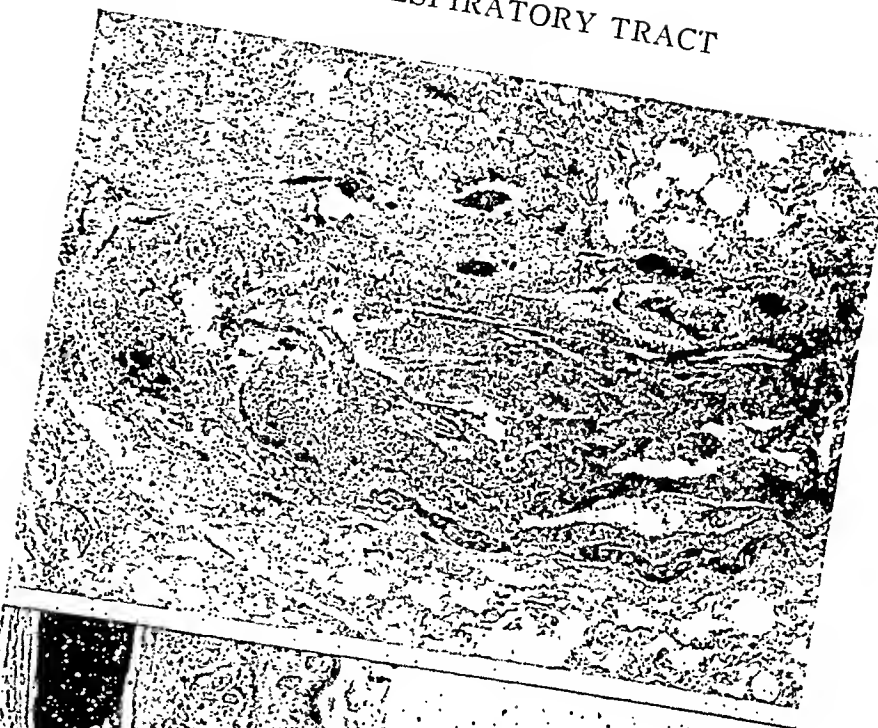


FIG. 29.—Segment of trachea just beneath the larynx from Case 7: The epithelial layer and basement membrane have been replaced by a hyaline fibrinous membrane. The underlying mucosa is thickened by edema.

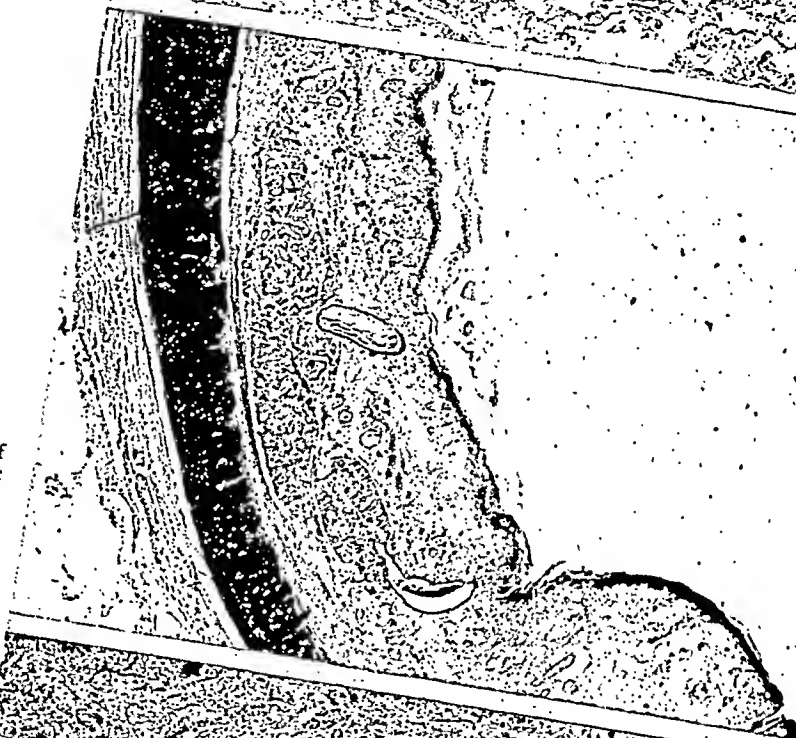
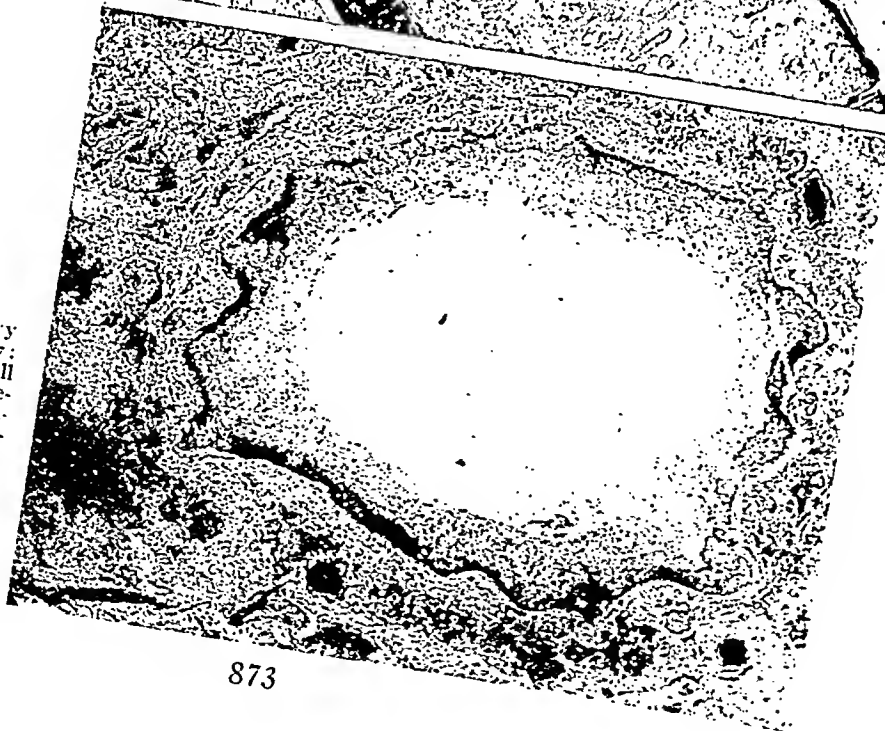


FIG. 30.—A tertiary bronchus from Case 7: The epithelial layer is still *in situ* but completely necrotic and partially hyalinized. On the left margin a small lake of serous exudate is present between the necrotic layer and the basement membrane. It is believed this represents the mechanism of spontaneous detachment of the necrotic tissues.



of the bronchial wall is markedly edematous and contains small numbers of scattered polymorphonuclears.

Bronchial Tree: The epithelial layer where visible is completely necrotic. In other areas it has desquamated leaving a denuded but intact basement membrane. Over considerable distances the shadow forms of the necrotic epithelial cells are visible as a distinct layer, sometimes still adherent to the basement membrane, more often partially separated from it by small lakes of serous exudate (Figs. 30 and 31). The lumina of most of the larger and all the smaller bronchi are plugged with casts composed of necrotic desquamated epithelium, polymorphonuclear leukocytes, monocytes often containing black granules, fibrin and traces of mucus in varying proportions. One bronchus contains a mass of cornified epithelial cells.

The deeper layers of the bronchial mucosa show maximal vascular engorgement and in some instances extensive interstitial hemorrhage. This frequently extends into the adventitia external to the cartilaginous rings. Leukocytes are usually concentrated just beneath the basement membrane and are scanty in the deeper layers.

Pulmonary Parenchyma: The picture varies widely in different portions of the lung. Throughout most of the lung the picture is one of physiologic emphysema alternating with edema and partial collapse. In the latter areas the alveoli average one-third to one-half the size of expanded alveoli, and are uniformly fluid-filled. No complete alveolar collapse is found. Even in the partially atelectatic areas, foci of trapped air are found in overdistended atria and respiratory bronchioles. The edema fluid for the most part has precipitated as an homogeneous, colloid-like mass in the alveoli. There are no fibrinoid membranes and little diapedesis of red cells.

Sections from the large hemorrhagic area (Fig. 32) described at the base of the left lung are somewhat unusual in appearance. The alveoli are uniformly small, one-third to one-half the size of those in neighboring areas. Their lumina are uniformly devoid of air as are also those of the atria and respiratory bronchioles. The majority are packed with red cells but others contain colloid-like edema fluid, and still others interlacing strands of fibrin; and all combinations of these three elements occur. Almost no leukocytes are present. The alveolar walls are perfectly preserved, their nuclei stain well and their capillaries can usually be made out and appear congested. The adventitia of all blood vessels in the zone is markedly hemorrhagic and packed red cells are found in many lymphatics.

Scattered throughout all lobes of both lungs, nonadherent hyaline emboli, similar to those noted in the superficial vessels of the larynx and trachea, are found in many of the pulmonary arterial branches. Other vessels, in the neighborhood of the hemorrhagic areas, show fresh, occlusive thrombi of the usual platelet and fibrin type.

Liver: Moderate fine, fat vacuolization is present in the hepatic cells of the central third of the lobule. In this same region slight edematous separation of the sinusoidal endothelium from the liver cords is evident.

Kidney: Negative.

Adrenal: The cell cords in the outer half of the fascicularis and inner glomerulosa show separation of the cells by pools of serous exudate in which a few strands of fibrin are frequently found. In an occasional focus there is complete interruption of the continuity of the cord where cells have completely disappeared. An occasional brightly eosinophilic cell with pknotic nucleus and a few foci of polymorphonuclear infiltration are found (Fig. 33).

Stomach: A section from the fundus shows marked vascular engorgement and scattered petechial hemorrhages in the mucosa.

Brain: There is disorganization of the Nissl substance of the cortical nerve cells. Scattered astrocytes in the cortex have swollen cytoplasm and two or three nuclei.

Fig. 1. Histological section of the respiratory tract showing a large, dark, circular lesion, possibly a cyst or abscess, surrounded by a dense cellular reaction.

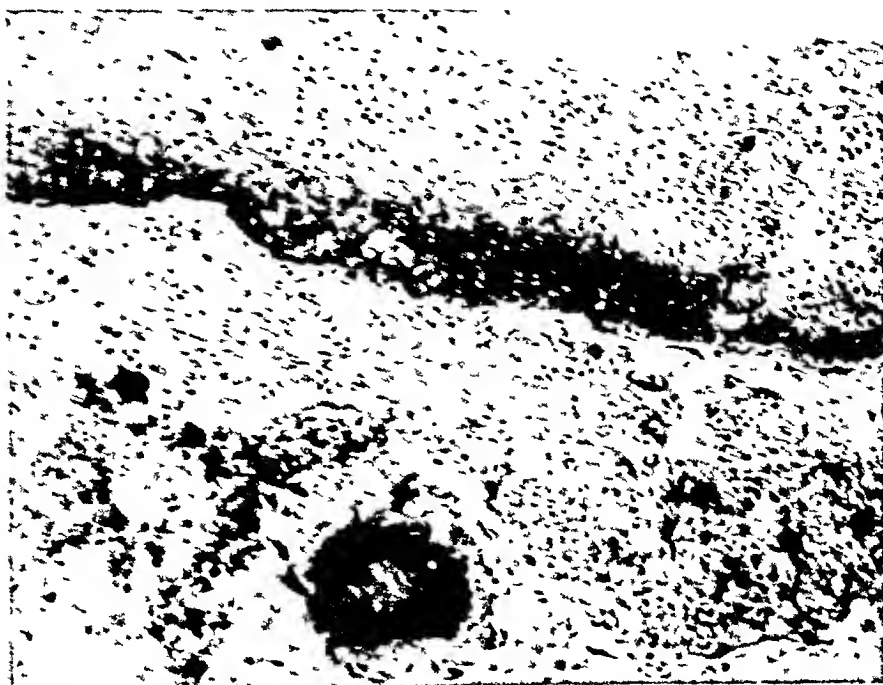
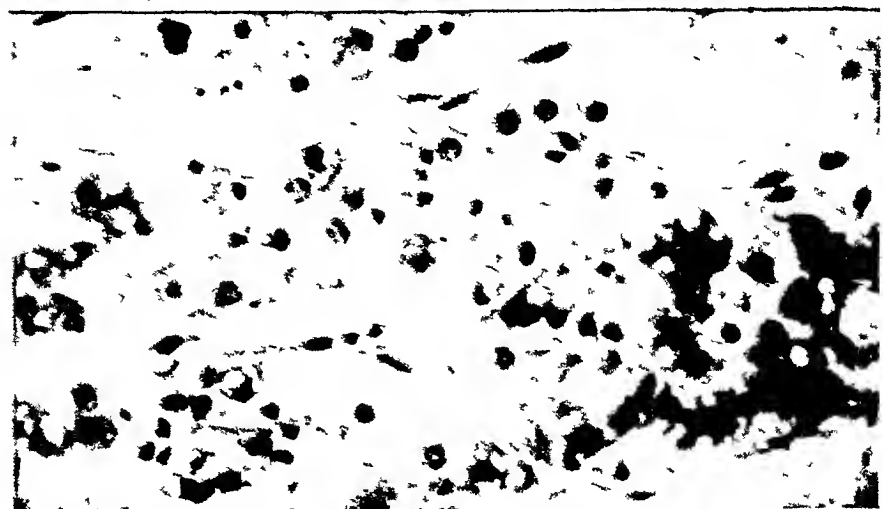


Fig. 2. Histological section of the respiratory tract showing a large, dark, circular lesion, possibly a cyst or abscess, surrounded by a dense cellular reaction.



Fig. 3. Histological section of the respiratory tract showing a large, dark, circular lesion, possibly a cyst or abscess, surrounded by a dense cellular reaction.



Marked satellitosis, such as is present in Case 27, is not observed, but sections from a corresponding region of the brain are not available.

Case 7, in summary, showed essentially the same type of membranous necrotizing inflammation of the larynx, trachea and bronchial tree as Case 25. In comparison, the process was somewhat more severe in the larynx (tracheotomy had been performed) and a little less intense in the bronchial tree. In contrast, the pulmonary changes were radically different. Whereas pre-existing anatomic emphysema and acute pulmonary edema dominated the picture in Case 25, in this one, atelectasis and compensatory physiologic emphysema were the rule. A complicating factor was provided by the extensive hemorrhagic lesions in the lower lobes. These are extremely difficult to interpret. Their gross configuration and their distribution conformed with the usual pattern of atelectasis, but the character of the cut surface seemed typical of infarction. Microscopic examination showed extensive hemorrhage into the alveoli compatible with infarction and multiple arterial emboli. However, the alveolar walls showed no necrosis and there was no trapped air within the lesion. No leukocytic infiltration was present, even at the margins.

The problem is to explain the massive alveolar hemorrhage. The picture was clearly not pneumonic. Blood aspiration from massive bronchial hemorrhage ordinarily presents a dispersed, fan-like pattern rather than the massive involvement present here. Furthermore, no clots were present in the bronchial tree and there was no history of massive hemoptysis. Simple atelectasis,¹ when based on bronchial occlusion, not on external pressure, is associated with serous exudate into the alveoli and moderate numbers of red blood cells may be present, but they never dominate the picture.

The final alternative is infarction. In very recent infarction sufficient time may not have elapsed to produce visible changes in the alveolar walls but in such early infarcts trapped air is almost invariably found. A condition known as partial infarction² must also be considered. This is a parenchymal injury based on arterial occlusion which does not go on to tissue necrosis because a collateral circulation develops within a comparatively short period. In this condition extensive hemorrhage into alveoli may occur, but again total displacement of air would be most unlikely. The final possibility to be considered is that infarction developed in a previously collapsed atelectatic area. This hypothesis would fit the gross appearances, but since the microscopic examination failed to show evidence of necrosis of alveolar walls it would be necessary to assume that it was very recent or that the infarction was but partial. The evidence does not warrant a definite diagnosis.

Another feature of note was the microscopic demonstration of adrenal cortical necrosis. This is of interest because of the physiologic evidence of change in adrenal cortical function obtained by Dr. Cope, and his associates, from study of the 17-ketosteroids excretion (metabolic observation). The brain showed histologic changes characteristic of anoxemia.

Case 27.—The body is that of a well-developed and well-nourished young woman, age 18. There are extensive superficial burns as follows: Third degree burns, the

PATHOLOGY OF THE RESPIRATORY TRACT

right side of the face, the forehead and the mouth. There is also a spot of third degree burn, 2.5 cm. in diameter, over the left malar bone. The margins of both ears are deeply burned and there is a second degree burn on the upper lip and most of the chin. Third degree burns cover the dorsum of both hands extending 4 cm. above the wrists and also the lateral aspect of both upper arms from elbows up to the acromion processes. The entire back from the buttocks up to the shoulders is completely covered by second and third degree wet, weeping lesions. Small scattered burns, each about 1 cm. in diameter, are found scattered along the anterior aspect of both lower legs overlying the tibial crests.

Trachea and Bronchi: Intense congestion is present without visible necrosis. There are scattered petechial hemorrhages in the upper trachea.

Bronchial Lymph Nodes: Slightly enlarged and wet.

Lungs (color section Fig. 8): Weight 1180 Gm. The lungs fail to collapse when the sternum is removed. Examined *in situ*, the lower two thirds of the left lower lobe is markedly atelectatic. The remaining portion of the lobe shows compensatory emphysema interrupted by a few scattered lobular areas of atelectasis. One transverse band of atelectasis, about 1 cm. in thickness, traverses the upper portion of the lobe at a level 5 cm. below the apex. Another band runs vertically at right angles to this up to the extreme tip of the lobe. On the lateral surface of this lobe adjoining the diaphragmatic margin is a purple area of sharply outlined consolidation, 3 cm. in diameter, over which petechial hemorrhages are found in the pleura. One centimeter posterior to this is a smaller similar nodule, 1 cm. in diameter. The left upper lobe is again predominantly emphysematous with readily visible alveoli but shows several scattered small patches of atelectasis ranging from 1 to 2.5 cm. in diameter. The right lower lobe shows massive atelectasis of the posterior two-thirds, whereas the anterior third is distended except for occasional purple lobular areas of collapse. A roughly spherical nodule of consolidation, 3.5 cm. in diameter, is present in the atelectatic portion on the lateral surface of the lung 2 cm. above the diaphragmatic border. The right middle lobe is predominantly emphysematous, with a focus of increased consistency near the lower anterior margin 3 cm. in diameter. This is light purple in color, there is no overlying pleural reaction. The right upper lobe is markedly emphysematous with a few small consolidated nodules, about 1 cm. in diameter, along the anterior margin.

A sagittal section of the right lung (color section Fig. 9) reveals marked congestion of the mucosa of the primary bronchus. Beginning in the lobar bronchi and becoming more intense in their secondary and tertiary subdivisions there is mucosal hemorrhage necrosis and pseudodiphtheritic membrane formation which extends even into the small bronchial radicles (color section Fig. 7). Large areas of red, depressed atelectatic tissue alternate with pale, aerated slightly overdistended parenchyma. Three sharply outlined foci, ranging from 1 to 3 cm. in diameter, extend inward from the pleura, which are deep red in color, very firm to palpation and have the gross appearance of infarcts. Thrombosed vessels are found in association with two of these.

Section of the fixed left lung shows essentially a similar picture. One area of apparently typical infarction is found on the diaphragmatic border. Approximately one-third of the upper lobe and two-thirds of the lower lobe are partially to completely atelectatic. In some areas the atelectatic tissue is firm enough to raise the suspicion of early consolidation.

Microscopic Examination—Trachea and Bronchi: An extensive superficial necrotizing process is present which never extends beneath the basement membrane. No normal epithelium is found. In a few areas necrotic shadow forms of epithelial cells lie in their normal positions still attached to the basement membrane. Frequently small pools of serum are found between the basement membrane and the necrotic layer, and in these areas all stages of desquamation are apparent. In many areas no traces of epithelium are left and the basement membrane is either bare or covered with a fibrinous

membrane containing numerous leukocytes. Interspersed with such areas are others where variable proportions of epithelium persist. Occasionally it is of nearly normal thickness but without recognizable differentiation into ciliated cells or goblet cells. Marked leukocytic infiltration is invariably present between the persisting cells. More commonly, the epithelial layer is thin and consists of one, two, or occasionally three layers of somewhat elongated oval or spindle-shaped cells whose long axes parallel the basement membrane (Fig. 34).

The deeper layers of the bronchial walls are invariably congested and occasionally hemorrhagic. The degree of leukocytic infiltration is not, however, great except for a narrow zone immediately beneath the basement membrane. Blood vessels within the bronchial walls are not thrombosed. The lumina of all medium-sized and small bronchi are more or less completely plugged with exudate. This consists in part of desquamated epithelium, in larger part of fibrinopurulent exudate intermixed with some masses of mucin. In one bronchus masses of cornified epithelial cells are found, presumably aspirated from higher in the respiratory tree. In another bronchus two large clumps of micrococci are seen.

Pulmonary Parenchyma: The picture is variegated, being compounded of intermixed atelectasis and physiologic emphysema, edema, pneumonia and focal infarction.

The edema is for the most part associated with partial atelectasis. The alveoli are smaller than normal but never completely collapsed and their lumina contain extensive granular deposits. In one respect, however, the picture varies from the preceding three cases. In many areas a brilliantly acidophilic fibrinoid membrane has formed peripheral to the granular material and in apposition with the wall of the air passage. These membranes are usually found in respiratory bronchioles and atria and comparatively rarely in alveoli (Fig. 35). In a few areas clusters of red blood cells are mixed with the granular precipitate.

The areas of infarction are lobular in size and the alveolar lumina are solidly packed with red cells. The alveolar walls are largely viable but in the center of the lesions they show early signs of necrosis. No trapped air is found in these foci, and bronchioles extending into them show no necrosis of their walls. One focus of partial infarction is found in which the alveolar lumina are packed with red cells and the capillaries contain hyaline thrombi but the alveolar walls are not necrotic. Throughout the lung, sometimes in comparatively normal areas, small, dense, usually nonocclusive thrombi are present in occasional vessels (Fig. 36). Two fresh fibrin and platelet thrombi are found in vessels 2-3 mm. in diameter. These are adherent to the walls and one shows traces of organization at the periphery.

The pneumonic foci (Fig. 37) tend to be peribronchial in one location. They show scrous precipitates, fibrin, red cells and numerous polymorphonuclear leukocytes. In some of the pneumonic foci, fibrinoid membranes are present and, again, are usually found in respiratory bronchioles and atria rather than in alveoli. Organisms are not numerous and are entirely intracellular. They appear to be cocci in pairs and short chains and are never lanceolate.

Adrenals: Distinct abnormalities are present. The cell cords, particularly in the outer half of the fascicularis, are frequently split and sometimes partially transected by spaces in which granular detritus has precipitated, indicating an accumulation of serous fluid. In these spaces mononuclear phagocytes are present in small numbers. In a few small and scattered foci acidophilic necrosis of adrenal cells is present and in these areas polymorphonuclears have collected (Fig. 38). The chromaffin cells of the medulla appear shrunken and the space between them and the sinusoidal endothelium is widened, suggesting edema.

Brain: The cerebral cortex is definitely abnormal. Many of the larger nerve cells including some of the Purkinje cells are surrounded by an increased number of satellite cells. Several mitotic glia cells are observed. Oligodendroglia cells in the

PATHOLOGY OF THE RESPIRATORY TRACT

FIG. 34. — A bronchus from Case 27: The lumen is plugged by desquamated cells, fibrin and leukocytes. For the most part the basement membrane is denuded but on the left some regenerating epithelial cells can be seen.

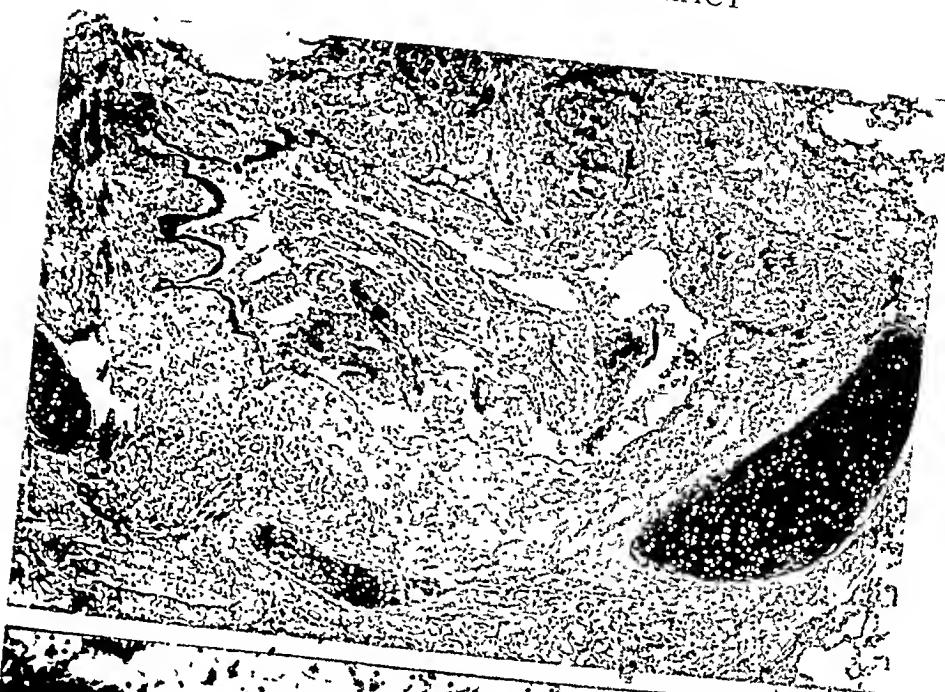
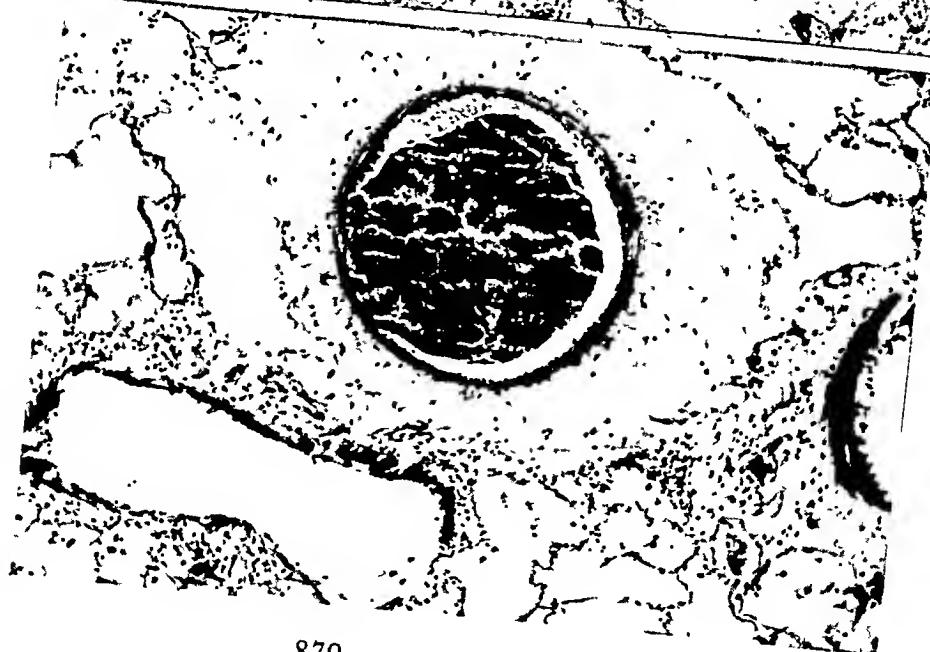


FIG. 35. — Case 27: Partially collapsed alveoli containing serous precipitate and a few leukocytes. The respiratory bronchioles are lined with an adherent fibrinoid membrane.



FIG. 36. — Case 27: An arteriole from a normal portion of the lung showing a nonadherent rather hyaline embolic occlusion. The perivascular lymphatic is widely dilated. Similar emboli were numerous in Case 7.



grey and white matter are swollen and those in the white matter are increased in number. Purkinje cells in the crowns of the folia have a disorganized Nissl substance and shrunken, deeply stained nuclei.

In summary this young woman was, like most of the female victims, much more extensively burned than the vast majority of the males but the extent of the cutaneous burns was hardly sufficient in itself to have caused death, especially in view of the prompt and vigorous therapy which she received. As in the two preceding cases, extensive pulmonary lesions appeared to be the major cause of death. Membranous bronchitis extended far into the periphery of the bronchial tree and atelectasis was more extensive than in any of the preceding cases. As in Case 7, multiple small emboli were demonstrable in many portions of the lung and several foci of dense lobular hemorrhage were present which seemed characteristic of infarction. Many more small foci of pneumonic infiltration were apparent on microscopic examination than had been recognized in gross. These occurred chiefly in areas of partial atelectasis and since the degree of leukocytic infiltration was not dense it seems probable that they were of comparatively short duration. Adrenal cortical necrosis was again apparent, as in Case 7, and the brain showed well-defined changes consistent with prolonged anoxemia.

SUMMARY OF POSTMORTEM FINDINGS

Six autopsies were performed upon victims of the Coconut Grove disaster. Three of these were upon bodies pronounced dead at the time of their arrival at the hospital and three upon cases which survived periods ranging from 40 to 62 hours. Common to all six cases were cutaneous burns of first, second and third degree of the exposed surfaces, the head and hands in all instances, and the shoulders, arms and back in the females who had worn low-cut evening gowns. In all cases the burns were particularly severe about the head. In the males the total area of cutaneous involvement was not great and even in the females it was certainly insufficient to have accounted for death within the brief period before the victim reached the hospital.

Postmortem examinations of the three cases dead on arrival showed a brilliant cherry-red discoloration of the muscles and of such blood-rich viscera as the lungs, liver and spleen, suggesting immediately the probability of carbon monoxide poisoning. Chemical determinations confirmed this surmise by demonstrating 42 and 50 per cent saturation of the hemoglobin with monoxide in two cases. In a third case, an effort was made to detect other poisonous products of combustion. The gaseous content of the tracheobronchial tree was aspirated under suction and analysis showed traces of oxides of nitrogen, a finding not confirmed by a second analysis.

All of the cases dead on arrival showed intense but nonnecrotizing hemorrhagic tracheitis and bronchitis, and all presented heavy voluminous lungs, from the cut surfaces of which fluid in large amounts could be expressed. Microscopic examination confirmed the presence of acute pulmonary edema and demonstrated in the upper tracheobronchial tree a serohemorrhagic exudation without significant leukocytic infiltration. It was concluded that

PATHOLOGY OF THE RESPIRATORY TRACT

FIG. 37.—Case 27: Focus of early broncho pneumonia.

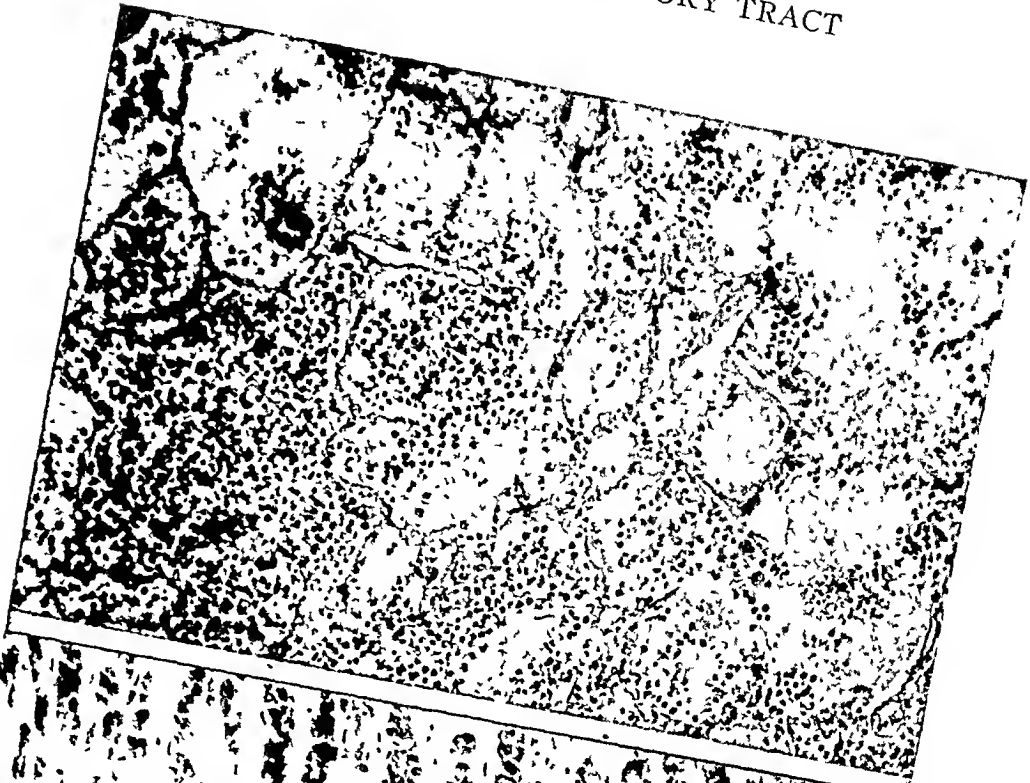
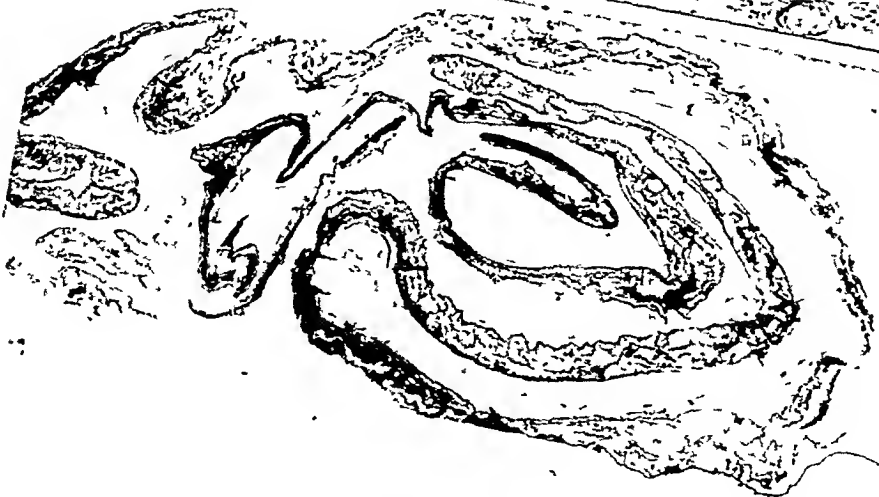


FIG. 38.—Case 27: Focal necrosis of the adrenal cortex. On the left the adrenal cells have been wholly resorbed, on the right they are vacuolated and there is monocytic infiltration.



FIG. 39. — A coil of broncholar membrane coughed up by a patient who survived.



the victims had inhaled an irritant agent, either physical or chemical, that they had lived long enough to develop a serous but not a leukocytic reaction, and that, therefore, their survival period was to be measured in minutes rather than in seconds or in hours. The mechanism of death was anoxemia, dependent in part upon inhalation of carbon monoxide and in all probability other gases, and in part upon edema of the lungs.

The cases which died after varying periods upon the wards showed similar distribution and extent of cutaneous burns. The major visceral lesions were again found in the respiratory tract. In Cases 7 and 25 severe



FIG. 40.—A higher magnification of the bronchial cast seen in Fig. 39. Note the necrotic respiratory epithelium in the separated membrane.

necrotizing laryngitis, with the formation of a pseudodiphtheritic membrane, had led to almost complete laryngeal stenosis. It is interesting that the process was most severe beneath, rather than above the vocal cords.

All three cases showed diffuse hemorrhagic and focal membranous reaction in the lower trachea and primary bronchi. All three showed diffuse membranous bronchitis most severe in the secondary and tertiary subdivisions of the lobar bronchi but extending in many areas to the smallest bronchioles. The membranes were found to be sometimes firmly adherent to the bronchial walls, sometimes readily separable. In many areas, notably in Case 7, the membranes had spontaneously separated and had coiled themselves within the bronchial lumina to form occlusive plugs. One of these, which was spontaneously raised by a patient who survived, is illustrated in Figures 39 and 40.

PATHOLOGY OF THE RESPIRATORY TRACT

Microscopic examination showed diffuse necrosis of the lining epithelium. In many areas the shadow forms of the necrotic cells rested *in situ* on the intact basement membrane. The accumulation of small lakes of serum between this layer and the basement membrane gave a clue to the mechanism of spontaneous detachment. In other areas all traces of the epithelium had disappeared and a dense, rather hyaline fibrinous membrane rested upon an intact basement membrane. In the larynx and trachea, but rarely in the bronchi, evidence of deeper necrosis was found and the basement membrane was itself partially or completely destroyed. Even in these areas the zone of necrosis was not deep, never wider than 100 microns. In Case 7, many of the vessels in and just beneath this zone were thrombosed.

In contrast to the fairly uniform changes in the tracheobronchial tree, the pulmonary lesions varied considerably from case to case. Case 7, a male age 29, showed severe anatomic emphysema, evidently of many years' standing. Superimposed upon this were an acute pulmonary edema and the barest traces of early bronchopneumonia. Case 25 showed extensive atelectasis and compensating physiologic emphysema. A complicating factor, which is difficult to interpret, was the presence of massive hemorrhage into the alveoli of large atelectatic areas, grossly suggesting infarction, but, microscopically, showing no necrosis of alveolar walls. The presence of multiple emboli throughout the pulmonary arterial tree provided the necessary precipitating factor and it is suggested that preexisting atelectasis may have been the substrate. In the aerated portions of the lung, in contrast, no reaction to the presence of the emboli could be detected. Case 27 was in many respects similar. Again atelectasis and compensatory physiologic emphysema dominated the picture. In this case, too, multiple small emboli were found throughout the lung in normal as well as in abnormal areas. Small foci of hemorrhage, usually only of lobular dimensions, were present, some of which were typical both grossly and microscopically of infarction; others showed viable alveolar walls like the lesions in Case 7. A further complicating factor was the presence of widespread foci of incipient bronchopneumonia within the areas of atelectasis. The very slight solidification of the lungs on gross examination, the predominant serous exudation, and the comparatively light leukocytic infiltration, all suggest that this pneumonic reaction was of very brief duration.

Other organs, with few exceptions, showed no abnormalities which could be attributed to the acute incident. The liver in Case 25 was markedly infiltrated with fat and that in Case 7 moderately so. In both instances the habitus of the patient suggested that its presence was physiologic. Careful examination of the kidneys showed no evidence of hemoglobinuric nephropathy, though this was found in several cases examined elsewhere in the city. The gastro-intestinal tract regularly showed congestion and petechial hemorrhages in the fundic portion of the stomach and in the duodenum. One parenchymal lesion could, it was believed, clearly be attributed to the acute injury. This was focal necrosis of the adrenal cortex, very

clearly demonstrable in Cases 7 and 27. In two cases the brain showed changes attributable to prolonged anoxemia.

DISCUSSION

Many of the facts of the Coconut Grove disaster are still shrouded in mystery, and it is not improbable that some of them will always remain so. It is clear that the victims were exposed briefly to flame of great intensity arising from inflammable material and, for a longer period, to toxic products of combustion which, in the enclosed space, may have reached high concentrations. Of the nature of the latter, nothing as yet is definitely known, beyond the demonstrated presence of carbon monoxide and at least traces of oxides of nitrogen. It may be assumed that both factors may have played a rôle in the pathologic lesions which were observed.

Testimony indicates that the flames were, to a considerable extent, limited to the upper portions of the various rooms. This checks with the pathologic observation that the heads of the victims were disproportionately burned. It also makes it understandable that inhalation of flame was frequent. How far flames may have penetrated into the respiratory passages is more difficult to determine with precision. Characteristic eschars were found within the nares; the black membranous exudation of the larynx, and the lesions in the trachea were probably of similar origin. The exaggeration of the necrotizing process below rather than above the vocal cords was presumably due to eddy formation below a point of narrowing. Lesions of this type are not unusual in the experience of a Medical Examiner.

More difficult to account for was the massive pulmonary edema which must have developed in an extremely brief period of time. Even with the most toxic war gases some latent period is usual, frequently a period of several hours. Anoxemia alone will rapidly produce pulmonary edema as Drinker, and his collaborators³ have shown. Perhaps a combination of anoxemia and some irritant vapor may have worked synergistically in these cases.

The most characteristic feature of the material was the diffuse membranous bronchitis. This is a characteristic effect of several of the war gases, notably phosgene, mustard gas and chlorpicrin.⁴ It is also characteristic of nitrogen dioxide inhalation.⁵ Herein lies the strongest pathologic evidence for inhalation of toxic fumes.

REFERENCES

- ¹ Loeschke, H.: Atelektase. Henke-Lubarsch Handbuch der speziellen Pathologischen und Histologie, Vol. III, Part I, page 603.
- ² Hampton, A. O., and Castleman, B.: Correlation of Postmortem Chest Teleroentgenograms with Autopsy Findings. *Am. J. Roentgenol. and Radium Therapy*, 43, 305-325, 1940.
- ³ Warren, M. F., Peterson, D. K., and Drinker, C. K.: Effects of Heightened Negative Pressure in the Chest Together with Anoxemia in Increasing the Flow of Lymph from the Lungs. *Am. J. Physiol.*, 137, 641-672, 1942.
- ⁴ Winternitz, M. C.: *Pathology of War Gas Poisoning*. Yale University Press, 1920.
- ⁵ von Oettingen, W. F.: *The Toxicity and Potential Dangers of Nitrous Fumes*. Public Health Bulletin No. 272, 1941.

THE TREATMENT OF THE SURFACE BURNS*

OLIVER COPE, M.D.

FROM THE DEPARTMENT OF SURGERY OF THE HARVARD MEDICAL SCHOOL, AND THE SURGICAL SERVICES
AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

UNTIL THE INTRODUCTION of physiologic methods of investigation into the clinic, the treatment of burns was merely the treatment of the surface wound. This was inevitable since the wound was obvious to physician and patient. In the last 50 years, with the recognition of hemoconcentration, the danger of the generalized shock of burns has been appreciated and an argument has developed within the profession as to which takes precedence in the treatment, the care of the surface wound or the care of shock. Even recently, men primarily interested in the shock picture say that nothing should be done to the surface until impending shock has been prevented or existing shock adequately treated.

Such emphasis on shock to the neglect of the surface treatment is wise if the surface treatment is one which leads to further shock. Débridement and cleansing under anesthesia is such a treatment. Débridement

Delay in the care of the surface wound, however, inevitably leads to bacterial contamination. With increase in contamination there is increased infection, and increased infection leads to shock as well as delayed wound healing.

Overemphasis on the surface treatment, to the neglect of that of shock and anoxia, and a tendency to attribute special virtues to a surface treatment, are also unenlightened. For example, when "toxins" were considered an etiologic agent in shock, tannic acid was advised on its presumed ability to fix *in situ* tissue toxins produced by the burn,¹ and reduction in the mortality of patients with burns has been ascribed to a surface treatment, whereas, in reality, it was due to better care of early shock.

The surface treatment cannot be divorced from the treatment of shock. It is the purpose of this article to outline a surface treatment which does not interfere with the life-saving treatment of shock yet tends to prevent bacterial contamination. This treatment is peculiarly suited to a catastrophe where the large number of burn casualties is out of proportion to the number of trained personnel. The problem of the therapy of shock is considered in a subsequent article.

THE SURFACE TREATMENT USED ON COCOANUT GROVE PATIENTS

Thirty-nine of the 114 patients brought to the Emergency Ward of the Massachusetts General Hospital from the Cocoanut Grove night club fire survived the initial few minutes and received treatment of their burns. Common to disasters, there was a pattern to the injuries. The burn pattern consisted of the hands, face, nostrils, mouth, the lower half of both corneas, and the scalp; and in the women, areas unprotected by adequate clothing, namely, the neck, arms, shoulders, back and legs. In addition to the pattern distribution, the back and legs of some of the men were burned. Burns

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

of all degrees were encountered, many having third degree or full-thickness burns.

The burns were sooty and shaggy, with unruptured blebs. Many were cherry-red color from carbon monoxide poisoning. Some of them looked clean, others grossly dirty. Many of the patients had been crawling on the floor at the fire, others had been dragged out from piles of dead. Many of the dead, and some of the unconscious who lived had been incontinent of both urine and feces.

But one type of surface treatment was applied to the burns of the skin of all of the 39 patients. A bland ointment with protective dressing was applied without any preliminary débridement or cleansing, and antibacterial chemotherapy was given internally.

As the patients entered the Emergency Ward, either walking or on a stretcher, sterile towels were placed over the burned surfaces. No covering was put over the faces. Insofar as possible these towels were held in place as the patients were undressed and transferred from stretcher to bed. For those patients having burns of the back, buttocks, and upper legs, sterile sheets were placed on the bed.

A needle was inserted for the intravenous administration of plasma before the dressings were applied to the burned surfaces. In many this was done while the patient was still on the stretcher.

When a patient was settled in bed, the sterile towels were folded back and the burn surfaces covered with sterile boric ointment strips. These strips were applied by interns or medical students who were not only capped and masked but were scrubbed and wearing rubber gloves. *The burn surfaces were neither cleansed nor débrided.**

The boric ointment gauze of fine mesh was covered with sterile gauze to protect the wounds. Burns of the face, scalp, and of the extremities were bandaged with pressure. This was accomplished by adding roller elastic bandages on top of the gauze dressing. Over the burns of the trunk, large stockinet rolls were applied. The dressings of burns of the neck were held in place by ordinary gauze bandages. The eyes, after application of 5 per cent sulfathiazole ointment, were closed and were included in the pressure dressings of the head. Only the nostrils and lips were left uncovered.

As a final part of the initial surface treatment, two grams of sodium sulfadiazine were injected intravenously through the cannula or needle already in place for plasma transfusion.

This surface dressing, and the chemotherapy, completed the care of the wound. It was first aid and definitive treatments combined. The dressings were not changed until the fifth to tenth day, when boric ointment gauze was reapplied. To those burns which proved to be of second degree, no other type of dressing was applied. To those areas later proving to have deep de-

* The face and left hand of one patient (Case 17) was partially débrided and cleansed with soap and water before applying a dressing of 5 per cent sulfathiazole ointment. This was done before the general order was appreciated.

TREATMENT OF SURFACE BURNS

struction of the skin, wet dressings of boric acid or physiologic saline solution were used after the first two weeks in order to expedite the removal of the burned tissue, and prepare the surfaces for grafting.

Rationale of the Surface Treatment Employed.—The use of this unorthodox surface treatment was premeditated and prompted by the concept that of treatments giving approximately equal results, the simplest would be the one best adapted for a disaster with numerous burn casualties.

No Débridement and No Cleansing.—We did not débride the burn wounds because we were convinced that the intact epidermis over the blebs protects against the entrance of bacteria, and because bleb fluid does not become contaminated by virulent organisms harbored in gland crypts.

We did not cleanse the burn surfaces because we believe that cleansing is ineffectual in reducing significantly the number of contaminating organisms present unless vigorous scrubbing is resorted to. Such scrubbing, it is believed, injures viable epithelium. An anesthetic also would be necessary and is undesirable from the point of view of augmenting shock.

The débridement of burn wounds, as commonly carried out, consists not only of picking off particles of clothing and other foreign material but also in rupturing any vesicles and removing the overlying epidermis and all of the loose epidermis of the vesicles already ruptured. This is ordinarily followed by cleansing. Admittedly, débridement is necessary for good tanning, and, therefore, débridement and cleansing are part of the tannic acid ritual; they have been carried over into other methods of treatment without criticism. These maneuvers are time-consuming as well as painful. They tie-up available personnel and require analgesic drugs, if not general anesthetics. The increased manipulation of the patient, prolonged exposure of the wounds, and anesthetics attendant with débridement, are conducive to serious shock. If these maneuvers can be eliminated, the trained personnel will be freed and the prevention of further shock accomplished.

When nondébridement of burn wounds was suggested soon after Pearl Harbor, serious objections were raised. It was maintained that all blebs must be opened because the bacteria harbored in the gland crypts at the base of the vesicle would swim up and infect the fluid.

On physiologic grounds the first objection seemed unreasonable. Superficial human burn wounds weep for many hours, and in dogs, Field, Drinker and White,² in 1931, showed that there was an increased flow of lymph induced by an experimental burn which continued for hours without clotting. These observations suggested a rapid turnover in the protein-rich fluid in the burn areas. The fluid comes from the plasma pouring through the open capillary membrane into the extracellular spaces and passes either out on to the surface or back through the lymphatics. Such a rapid turnover of plasma fluid should mean a relatively high oxygen content of the edema fluid in the burn area.

Against the second objection are the bacteriologic observations of Colebrook,³ and others,^{4,5} pointing to the ability of skin to rid itself of patho-

genic bacteria. There are normal habitants of skin which are not sufficiently virulent to cause infection, and little trouble is to be expected from these. Virulent bacteria are destroyed, perhaps by the skin lipoids.⁵ The heat producing the burn also decreases the number of bacteria present on the skin at the time.

Finally, it remained to find out in patients with burns what happened to the fluid of, and healing beneath, the unruptured vesicles. Twenty-six patients had been studied prior to the Cocoanut Grove fire. The fluid from more than one bleb was observed in many of the patients. In those arriving at the hospital with unruptured blebs, the blebs were protected by gauze to prevent rupture. Many of the patients' burns were hours to days old when first seen, and the blebs had not been protected from contamination by any dressing. From 24 hours to 14 days after the burn the fluid was removed from the vesicles under sterile precautions and cultured in Dr. Champ Lyons' laboratory. In a few instances, the nonpathogenic saprophytic organisms of normal skin were recovered. In only one instance was a pathogenic organism, a *beta* hemolytic streptococcus, obtained in fluid of an unruptured bleb, and in this case alone was the fluid purulent. It was the clinical impression that the healing beneath the unruptured blebs occurred as rapidly as under any of the agents commonly recommended for the burn surface.

Another objection which has been raised to nondébridement is that the dead epidermis of vesicles which have already ruptured provides a culture medium for organisms. Such broken epidermis usually retracts and is often found rolled up in a corner of the old vesicle. Admittedly, it looks messy and unsurgical, but how dangerous a culture medium is it and what do we accomplish by taking it away? If it is excised and a dressing applied, it will be replaced by a layer of fibrin between cells and dressing. As far as is known, this inert fibrin is as good a culture medium as the dead epidermis. Since unruptured vesicles are not infected, the under surface of the broken epidermis is presumably uninfected. Even though it now covers a lesser surface of the burn, it is still a protection and as physiologic as any that is now known.

A major point in favor of nondébridement of the burn wound is, as has been shown in this laboratory, the availability to the wound of chemotherapeutic agents administered internally. Absorption of sulfonamides applied locally to the débrided burn surface has been observed at this hospital by Dr. Lyons, and also reported in the literature. Such absorption may be rapid and irregular and if the burn surface is large, toxic levels of the drugs in the body fluids may be reached. (Absorption from a nondébrided surface has not been measured.)

The levels of the sulfonamide drugs in the body fluids are more easily controlled by internal administration. Therefore, if it could be shown that these drugs permeate through the burn tissue, this route would be preferable. Since sulfonamides are freely diffusible and there is an increase in capillary permeability in the region of the burn with delayed clotting of the edema

TREATMENT OF SURFACE BURNS

and bleb fluid, it seemed likely that free diffusion, in the early hours at least, would be found.

As anticipated, the level of the sulfonamides in the bleb fluid of unruptured vesicles followed closely that of the blood plasma. For example, a girl with a burn of the leg and a large unruptured bleb was started on sulfadiazine by mouth two hours after the burn. Twelve hours later a titer of 4.3 mg. of the drug was found both in the bleb fluid and blood plasma. Such observations were repeated on a number of the Coconut Grove fire patients.

It is not known for how long sulfonamides, administered internally, permeate freely through the burn wound. Fibrin is eventually deposited in the intercellular spaces of the wound and it is probable, when this stage of the inflammatory process is complete, that substances normally diffusible are no longer able to permeate through the wound in a patient treated since the Coconut Grove disaster. A hot water burn of the lower leg resulted in a large unruptured bleb. Sulfadiazine was withheld until 60 hours after the burn. At 73 hours the levels of sulfadiazine were 8 mg. in blood and 3.3 mg. in the bleb fluid. The time limit, if such exists, remains to be determined.

It seemed reasonable on the basis of these findings in the fluid of unruptured blebs (absence of virulent bacteria, good healing in its presence, and availability to it of internally administered sulfonamides) to treat burn patients with the greatly simplified surface treatment of no débridement, no cleansing, and a simple bland ointment with protective dressing. Several patients had been treated in this manner prior to the Coconut Grove disaster and the observations on them afforded an adequate basis for planning to use such a simplified treatment in a disaster with numerous burn casualties.

Boric Ointment: A bland, protective ointment dressing is indicated in the treatment of skin burns since the chemical agents currently recommended are believed to be injurious to otherwise viable epithelium and delay wound healing. In a previous communication from this hospital,⁶ it has been shown that tannic acid, the dye solutions, and certain other preparations delay the healing of an epithelial wound. Use was made of the donor site, from which a skin graft of uniform thickness had been removed by the dermatome, for the assay of these various agents. This wound heals by epithelial proliferation with a minimum of fibrous tissue contracture. It is also a sterile wound and the retarding influences of various infectious organisms is eliminated as a complicating factor. Although it is not a burn wound and does not have the superficial layer of dead tissue created by the burn, from the point of view of healing it has much in common with the burn wound. Substances retarding healing in this donor site wound would presumably have the same action on the viable epithelium of a burn wound.

It is difficult, if not impossible, to assay accurately the effect of a chemical agent on epithelial regeneration using a clinical burn wound. There are factors other than the substance applied locally which influence

the rate of healing. There is no proven clinical method of judging accurately the extent to which the cells are damaged by the burn, and thus no two burned areas can be considered of identical depth or degree. Obviously, the deeper the burn, the slower the healing will be. Also complications of the burn, infection and malnutrition, delay the eventual healing. The effect on healing ascribed to an agent may be due in reality to the depth of the burn or to other factors.*

Boric ointment gauze was used as the control agent in these experiments upon epithelial regeneration. It is chiefly because this ointment is commonly used in hospitals for many purposes that it has been chosen for treating burns. Dr. Lyons feels that the boric acid in the ointment may inhibit the growth of the pyocyanus organism. (It is known to rid granulating wounds of pyocyanus infection.) The relative absence of this organism in the wounds in the patients treated in the disaster is a possible confirmation of this effect. It should be pointed out, however, that little is known regarding the absorption of boric acid from burn or granulating surface wounds, and since boric acid has been occasionally reported to give rise to toxic symptoms, it may prove wise, after further investigation to omit the boric acid and use plain petrolatum for burns. In this way, excessive absorption from large areas would be avoided.†

A bland ointment usually gives prompt relief of pain. Apparently any oily substance, perhaps because it excludes air from the wound, is comfortable. If pain persists, it may be due to too tight a dressing.

Pressure Bandage and Splinting.—The indications for the use of pressure dressings on the extremities and face are not clear to us. Pressure dressings on the extremities do prevent the occurrence of massive edema beneath the bandages but may not prevent the loss of plasma. In the patients of the Coconut Grove disaster, the fluid which seeped out in the burned hands, and which would have formed edema locally, was expressed up the arm and produced massive edema. Edema of the burned faces developed despite the pressure dressings. Where the scalp was not burned in addition to the face, edema fluid from the face was expressed posteriorly and a generalized edema beneath the bandage was produced. Edema fluid was also expressed downwards into the soft tissues of the neck and over the shoulders and upper chest (color section Fig. 15 b). (Massive edema of the breasts devel-

* The solutions of both tannic acid and the triple dyes recommended for the treatment of burns are strongly acid, pH 2.0 and 2.5, respectively. Neutralized solutions were not tried. It is possible that the retardation of healing was due to the acidity rather than to anything specifically involved in the tannate or the dyes.

† Since this article was written, the urine of 20 of the patients has been analyzed for boric acid. A maximum of 2 Gm. was excreted in 24 hours in the first two days in the patients with extensive burns. Later on when boric acid solution was used to irrigate the granulating wounds, as much as 2.5 Gm. were excreted in the urine in 24 hours. These levels are far below those of excretion reported in patients having toxic symptoms from boric acid poisoning. Since all our patients maintained normal kidney function it is probable that the excretion of boric acid was prompt, toxic levels from absorption were not approached, and the use of boric acid in petrolatum is safe.

TREATMENT OF SURFACE BURNS

oped in Case 13.) Distended, edematous tissues were encountered, on performing a tracheotomy where there was no superficial burns of the neck. It is of course possible that an excessive edema beneath a burn wound may tend often to increase tissue damage. On the other hand, we have no evidence that healing was expedited in any of our cases by the use of pressure dressings.

Splinting of an extremity is comfortable and rolled newspapers were incorporated in an outer layer of the pressure dressings. Such splinting decreases lymph flow which may not be of benefit in a sterile burn wound but is in a septic wound. Lymph stasis facilitates the localization of the septic process.

Administrative Advantages of a Simple Treatment.—From the administrative point of view in handling casualties of a disaster there are many advantages of a simple treatment. The problems of personnel are the most important. In battle or in a civilian disaster there is inevitably a disproportionate number of trained medical personnel required to administer it. The treatment used on the patients at this hospital from the Coconut Grove fire can be applied by nurses or orderlies. Physicians present are freed for the administration of plasma for shock, and oxygen for anoxia. The operating room and a general anesthetic are dispensed with. The operating room facilities are freed for the care of other injuries. This hospital had seven operating rooms, with personnel, in preparation for the patients of this fire. When it was obvious that no injuries requiring operative treatment had been sustained, the personnel was made available for other work. There is no theoretic reason why burn wounds should have both first aid and definitive treatments. The elimination of the definitive treatment, a relic of the tannic acid regimen, spares much wasted effort on the part of personnel and discomfort to the patient.

Another advantage of a simple treatment from the administrative point of view is the problem of equipment, supplies, and their storage. Ideally, nothing should be required for the treatment of a burn which is not also useful for some other type of wound. The substances required for the treatment described are useful in other types of injuries. In contrast, the paraffin treatment with its heater and spray-gun complicates the requirements and rules out this method even though it may give equally good results. Tannic acid and triple dyes have not been recommended for injuries other than burns. Such considerations of equipment are of paramount importance to the Army and Navy where transportation and storage are problems.

Medical Advantages of Simplicity.—The treatment of a heat burn should, ideally, be directed toward the prevention of its complications. Of these the most important are infection and shock. Since infection originates almost entirely from contamination with organisms arriving on the burn surface after the burn has occurred, the earlier the wound is protected, the less will be the infection. It is clear that the simpler the treatment, the sooner it can be applied.

Infection is to be avoided not only because of the shock due to infectious toxemia but also because it delays wound healing and adds to scarring. Indeed, it is probable that the growth of various organisms on burn wounds destroys otherwise viable epithelium and may convert a deep second degree burn into a full-thickness destruction of the epithelium. From the point of view both of survival and early convalescence, infection is most objectionable.

The simpler the treatment, the less manipulation there will be of the patient. From the point of view of aggravation of shock this is important. The rolling of the patient, incident to débridement and washing, not only increases pain but disturbs further the circulatory imbalance impending in shock. Since a simple treatment with minimal requirements of materials will be applied earlier, quicker relief of pain will be obtained, and this too helps to prevent shock.

Results.—The results of the treatment of the burn surface have been considered by the Staff as gratifying. The second degree burns healed promptly without evidence of infection, and with minimal scarring. Examples are shown in the colored photographs (color section Fig. 13 a-e. and color section Fig. 15 a-e). Of the deep burns, the wounds remained unusually free of active or invasive infection. In his article, Dr. Lyons details the course of bacteriologic flora of the wounds and the success of the chemotherapy. Cultures of the burn wounds were not obtained until the time of the first change of dressings so the amount and nature of the contamination present at the time of entry is not known. The subsequent lack of invasive infection was presumably due to the chemotherapy rather than to any unusual cleanliness of the burns on arrival for they were grossly dirty, and there were many chances for fecal and respiratory tract contamination before arrival at the hospital.

Clinical proof that the original surface treatment used, did not lead to infection, and, indeed, on the contrary, was effective in checking the growth of organisms which were present, is shown by the experience with the left hand of Case 2 (color section Fig. 14 a-j). Two extensor tendons were exposed on the dorsum of the hand and Dr. Cannon elected to graft the hand by burying it in the abdominal wall. Had there been active infection in this wound the tendon would not have survived, the graft would not have become attached, and the abdominal wall wound would have suppurated.

On the fifteenth day after the disaster, the isolation floor was closed. Sixteen patients by this time had been discharged home with lungs free of signs and with surface burns healed. Another patient with a small third degree burn of an ankle had been discharged on the fourteenth day to a Naval Hospital, the second degree burns having healed. (Seven patients had died as the results of the pulmonary complications.)

Of the 15 patients left in the hospital, four were held for residual pulmonary signs, the second degree surface burns of three having healed. (The fourth had no surface burns). These four were discharged from the seventeenth to the thirty-second day.

The patient with the central nervous system damage from anoxia re-

TREATMENT OF SURFACE BURNS

mained, the minor burns having healed by the tenth day. She was discharged on the sixty-seventh day. The remaining ten patients were those with the third degree burns. Dr. Cannon describes in his article the wound healing observed in these. The last of these was discharged on the one hundred and forty-third day.

COMMENT.—The problem of débridement and cleansing cannot be categorically answered for all burns. If a burn surface has been rubbed in dirt, more infection may be avoided by débriding and cleansing. In some cases a sluice of water over the surface without débriding may be nearly as effective as any other method. The point to emphasize is that neither débridement nor cleansing are essential to the good care of burns. Good surgical judgment in their care, as in that of many other diseases, consists of knowing when not to interfere.

The advisability of using pressure dressings on extremities and face has not been settled by the care of the patients of the Cocoanut Grove fire at this hospital. The dressings undoubtedly tend to restrict the loss of plasma and, therefore, the decrease in plasma volume but they do not prevent it, particularly in deep burns of the face and scalp when the edema fluid collects in the neck and over the shoulders and chest. A point more important to settle than the effect of pressure on the loss of plasma volume, however, is whether local edema of the burn tissue is harmful and whether pressure improves the local nutrition. We have obtained no objective evidence on this point.

CONCLUSIONS

A treatment for the surface wounds of burn casualties is described and its rationale discussed. It consists of no débridement, no cleansing, a bland ointment with protective dressing and internally administered chemotherapy. It was given extensive trial on the surface burns of the casualties from the Cocoanut Grove fire treated at the Massachusetts General Hospital and proven eminently satisfactory. Its advantage lies in its simplicity. The available personnel is freed for the care of shock and anoxia, yet the surface wounds need not be neglected.

REFERENCES

- ¹ Davidson, E. C.: Tannic Acid in the Treatment of Burns. *Surg., Gynec. & Obst.*, **41**, 202, 1925.
- ² Field, M. E., Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation. *J. Exper. Med.*, **56**, 363 1932.
- ³ Colebrook, L., and Maxted, W. R.: Antisepsis in Midwifery. *J. Obst. Gynec. Brit. Emp.*, **40**, 966, 1933.
- ⁴ Jennison, M. W., and Sizer, I. W.: The Disappearance of Bacteria Applied to the Human Skin. *From Report of Proc. Third Internat. Congress for Microbiology*, p. 259, 1939.
- ⁵ Burtenshaw, J. M. L.: The Mechanism of Self-Disinfection of the Human Skin and its Appendages. *J. Hygiene*, **42**, 184, 1942. *Idem*: Mortality of Haemolytic Streptococcus on Skin and on Other Surfaces. *J. Hygiene*, **38**, 575, 1938.
- ⁶ Cannon, B., and Cope, O.: Rate of Epithelial Regeneration. *ANNALS OF SURGERY*, **117**, 85, 1943.

PROBLEMS OF INFECTION AND CHEMOTHERAPY*

CHAMP LYONS, M.D.

FROM THE DEPARTMENT OF SURGERY OF THE HARVARD MEDICAL SCHOOL AND THE SURGICAL SERVICES OF THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

THERE is probably no surgical wound more difficult to evaluate from the point of view of bacterial infection than a deep burn. It is impossible to assess the depth and extent of the fresh burn, and a large number of different types of bacteria are recoverable from the burn surface. During the phase of healing it is frequently impossible to determine to what extent the bacterial contamination has contributed to tissue necrosis. The pathogenicity of certain bacteria may be obvious but with others there may be considerable question. Bacteria which, in pure cultures, are classified as saprophytes may in mixed cultures be pathogens in consequence of synergism. It is usually difficult or impossible to determine the quantitative aspect of the initial contamination or the resistance of the host.

TABLE I
SULFONAMIDE BLOOD LEVELS DURING THE FIRST TEN DAYS OF TREATMENT

Level mg. %	Initial	Subsequent	
		Minimal	Maximal
Less than 2	0	2	0
2—3	2	5	2
3—4	2	6	1
4—5	12	14	1
5—6	6	0	2
6—7	1	0	5
7—8	5	1	8
8—9	2	0	4
9—10	0		2
10—11			3
11—12			0
Total No. of patients	30	28	28

Certain principles of treatment were agreed upon during the period of arrival of the first patients. In general, it was held that:

1. The prevention and treatment of shock must be the first and immediate consideration.
2. Further contamination of wounds must be avoided.
3. Measures to control the established bacterial contamination would be limited to increasing the resistance of the host by chemotherapy, passive immunization and maintenance of nutrition.

The rôle of shock in infections cannot be overemphasized. The hemolytic streptococcus is frequently a preferential anaerobe,¹ and one of its lethal toxins is oxygen-sensitive.² The importance of shock in gas gangrene, and *vice versa*, was well recognized in World War I. Any factor which retards the circulation and lowers tissue oxygenation invites anaerobic growth of

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and the Massachusetts General Hospital.

INFECTION AND CHEMOTHERAPY

bacteria. Tetanus was a special risk of the thermal trauma from frostbite in the Russian army during the Finnish campaign.³ On the other hand, postoperative shock is often the outward manifestation of hemolytic streptococcus wound infection.⁴ Hence, it would appear that the prophylaxis of infection is an integral part of the shock problem as it applies to burns. Clinical experience with established infections indicates that an effective blood level of sulfonamide offers the most certain control of systemic infection due to the hemolytic streptococcus. The prompt intravenous administration of a known amount of sulfonamide seemed to be the most direct method of combating shock due to infection.

TABLE II
COMPLICATIONS ATTRIBUTED TO SULFONAMIDE THERAPY FOR SEVEN OR MORE DAYS

Complications	No. Patients
Hematuria* only.....	14
Crystalluria only.....	3
Hematuria* and crystalluria.....	9
Fever	2
Fever and rash.....	2
Agranulocytosis.....	1
* Microscopic	

In recording this clinical experience with the victims of the Cocoanut Grove fire every effort has been made to distinguish between factual data and inference from clinical observations. It seems wise to maintain this distinction here.

FACTUAL DATA

Asepsis and Sterile Precautions.—A strictly aseptic technic was not practical for the initial reception of the patients. All hospital attendants in the receiving ward were masked but it was impossible to mask patients because of the face burns and respiratory difficulties. Clean unsterile gowns

TABLE III
TEMPERATURE RESPONSE 72 HOURS AFTER STARTING PENICILLIN

Case No.	Diagnosis	W.B.C.	Maximal Temperature Degree Fahr.	
			5th Day	9th Day
19	Pulmonary burn.....	15,400	102	100.5
32	Pulmonary burn and CO poison.....	13,000	102	101
2	Pulmonary and deep burn.....	12,600	104.5	100.5
8	Pulmonary and deep burn.....	27,000	103.5	101.5
11	Pulmonary and deep burn.....	13,000	104	102.5
13	Pulmonary and deep burn.....	25,400	103	102
20	Pulmonary and deep burn.....	17,000	102	103
23	Pulmonary and deep burn.....	24,000	102.5	101.5
28	Pulmonary and deep burn.....	20,000	102	101.5
36	Pulmonary and deep burn.....	13,800	102	101.5
38	Pulmonary and deep burn.....	26,000	102	102

were donned by volunteer assistants in street clothes but this was not universal. Hospital attendants wore their usual clothing without other covering. Morphine sedation and intravenous fluid therapy were started as soon as possible after arrival. The rapid transfer of patients from the receiving ward to the ward isolated for their care facilitated supervision of sterile precautions. At-

tendants here wore clean unsterile operating room clothes, caps, masks, and rubber gloves. The gloves were sterile initially but these were contaminated from wound to wound and from patient to patient. Hospital supervisors and directors as well as military officers were admitted to the ward when masked. As soon as clothing was removed from patients the burns were covered with sterile boric ointment strips and sterile gauze under a pressure dressing. The materials used for this purpose were originally sterile but much cross-contamination occurred in the process of application of the dressings.

With the occlusive dressing in place, attention was focused chiefly on the masking of attendants and the "isolation" of the patients. The burn ward was established as a complete hospital unit. One solarium was set up for roentgenologic examination and another was converted into an

TABLE IV
CASE 2: DISCHARGED ON 87TH DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Treatment:									
Penicillin									
Sulfadiazine									
Organisms:									
Staph., coag. +.....	+	+	+	+	+		+		+
Staph., coag. —.....	+	+	+						
Beta strep., group A.....									
Beta strep., other.....			+						+
Alpha strep.....	+								
Gamma strep., aer.....									
Gamma strep., anaer.....									
<i>E. coli</i> , etc.....		+	+						
<i>B. pyocyaneus</i>			+						
<i>B. proteus</i>				+	+		+		
<i>Cl. welchii</i>	+	+							
Other Clostridia.....									
Diphtheroids.....	+	+	+		+		+		+
<i>B. subtilis</i>	+	+		+					

operating room for the change of dressings with complete aseptic technic. Entrance to the ward was allowed only to those directly concerned with the care of the patients. In general, families and visitors were excluded, but family physicians, sectarian religious advisers and accredited investigating scientists and physicians were admitted to the ward by appointment. Admission to the operating room for observation of wounds during dressing periods was restricted to those persons necessary for the immediate problem of changing the dressing, photography, and bacteriologic study. Throat cultures were taken on all visitors to this operating room and the room was thoroughly cleansed and set-up again before each change of dressing.

The Prophylaxis and Treatment of Infections.—Sulfonamide Therapy: About two hours after admission the patients were in bed on the isolation ward with bandages in place and intravenous fluids started. A single technician was given a flask of 5 per cent sodium sulfadiazine in sterile distilled water and a sterile 50 cc. syringe; 2 Gm. of sodium suladiazine in 40 cc. solution were injected into the rubber tubing of each intravenous set. The injection was assured of prompt conveyance to the vein by

INFECTION AND CHEMOTHERAPY

occluding the rubber tubing momentarily just distal to the injection site. Subsequent chemotherapy was planned for 4 Gm. daily, either as one gram every six hours by mouth or two grams twice daily intravenously. Aliquot portions of soda bicarbonate were not given initially but were administered for later hematuria or crystalluria.

CASE 8: DISCHARGED 63RD DAY. REQUIRED SKIN GRAFTING

Weeks.. :	1st	2nd	3rd	4th	5th	6th	7th
Treatment:							
Penicillin							
Sulfadiazine							
Organisms:							
Staph., coag. +	+						
Staph., coag. -		+					
Beta strep., group A		+	+	+	+	+	+
Beta strep., other							
Alpha strep.							
Gamma strep., aer.	+		+	+	+	+	+
Gamma strep. anaer.		+					
<i>E. coli</i> , etc.			+	+			
<i>B. pyocyaneus</i>							
<i>B. proteus</i>							
<i>Cl. welchii</i>					+		
Other Clostridia	+		+				
Diphtheroids	+	+	+	+	+	+	+
<i>B. subtilis</i>	+	+	+	+	+	+	+

CASE 11: DISCHARGED ON 103RD DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th
Treatment:								
Penicillin								
Sulfadiazine								
Organisms:								
Staph., coag. +	+							
Staph., coag. -		+						
Beta strep., group A	+	+	+					
Beta strep., other		+						
Alpha strep.			+	+		+		
Gamma strep., aer.	+						+	
Gamma strep. anaer.		+						
<i>E. coli</i> , etc.								
<i>B. pyocyaneus</i>								
<i>B. proteus</i>								
<i>Cl. welchii</i>		+	+					
Other Clostridia								
Diphtheroids	+		+	+	+			
<i>B. subtilis</i>	+	+	+	+	+	+	+	+

Thirty of the 39 patients survived or remained in the hospital long enough to have blood determinations of the sulfonamide level on the morning of the second hospital day.* The blood levels of sulfonamide during the first ten days of treatment are summarized in Table I.

* The first actual determinations of sulfadiazine levels of the blood were made on the second day. Subsequently, sulfadiazine levels were determined on samples of blood left from the first day in nine patients. In three of these the blood levels showed no sulfadiazine or only a trace. In the others the range was from 3.1 to 13.2 mg. per cent. In the three patients whose blood was measured three hours after the initial injection of sulfadiazine, the levels were 0, 7.9 and 9.1 mg. per cent.

In this group of patients the level varied roughly between four and ten mg. per cent. No patient developed an abnormally high blood level. The maximal period of treatment was 134 days in one patient.

The complications attributed to sulfonamide therapy in 26 patients receiving drug for seven or more days are listed in Table II.

It was necessary to administer alkali and alter dosage to control hematuria and crystalluria but no patient developed costovertebral tenderness or anuria. The drug had to be omitted in five patients: Two with fever; two

TABLE VII
CASE 13: DISCHARGED ON 143RD DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th
Treatment:								
Penicillin								
Sulfadiazine								
Organisms:								
Staph., coag. +.....	+	+	+	+	+	+	+	
Staph., coag. —.....	+		+	+			+	
Beta strep., group A.....	+	+						
Beta strep., other.....								
Alpha strep.....	+	+		+				
Gamma strep., aer.....				+		+		
Gamma strep., anaer.....								
<i>E. coli</i> , etc.....		+						
<i>B. pyocyaneus</i>						+		
<i>B. proteus</i>			+	+	+	+	+	
<i>Cl. welchii</i>				+				
Other Clostridia.....				+	+	+	+	
Diphtheroids.....	+	+	+	+	+	+	+	
<i>B. subtilis</i>	+	+	+	+	+	+	+	

with rash; and one with agranulocytosis. Agranulocytosis was apparent in Case 20 on the twenty-fifth day. Sulfadiazine was promptly omitted. The white blood cell count dropped to 1,000 on the twenty-sixth day, and she was started on pentnucleotide therapy. She had been receiving penicillin since the sixth day and its administration was continued. There was a prompt remission of the agranulocytosis by the thirtieth day, when the white blood cell count had returned to 8,500.

Tetanus Prophylaxis: Members of the armed forces remaining in the hospital for more than two days received "booster" doses of tetanus toxoid. Civilians were skin-tested with a 1:10 dilution of horse serum the morning after admission, when shock was obviously controlled. No positive reactions were observed and 3,000 units of tetanus antitoxin were given all civilian patients with surface burns, with three exceptions. The exceptions were individuals with severe respiratory difficulty in whom it was desirable to avoid any risk of bronchospasm.

Penicillin Therapy: Eleven patients were noted on the sixth day to have temperature elevations to 101° F., or higher by rectum. In many of these a real leukocytosis was present. In spite of the clean appearance of the wounds, it was felt that infection was probably present to produce these changes. Coagulase-positive staphylococci had been demonstrated to be the predominant pathogens in the respiratory tract of the patients dying of respiratory obstruction and similar organisms had been recovered from the

INFECTION AND CHEMOTHERAPY

throats of many of the surviving patients and attendants. The problem was discussed with Dr. Chester S. Keefer who agreed that penicillin therapy might be helpful. A dosage plan of 5,000 units every four hours intramuscularly was selected. The first concentrations contained 5,000 units in 5 cc. of physiologic salt solution but these caused considerable discomfort

CASE 20: DISCHARGED 84TH DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th
Treatment:								
Penicillin								
Sulfadiazine								
Organisms:								
Staph., coag. +.....	+	+	+	+	+	+	+	+
Staph., coag. -.....	+	+	+	+	+	+	+	+
Beta strep., group A.....		+						
Beta strep., other.....		+						
Alpha strep.....			+		+	+	+	+
Gamma strep., aer.....	+				+			
Gamma strep., anaer.....					+			
E. coli, etc.....						+		
B. pyocyaneus.....						+		
B. proteus.....			+	+				
Cl. welchii.....				+		+	+	
Other Clostridia.....	+					+	+	
Diphtheroids.....	+				+			+
B. subtilis.....	+	+	+	+	+	+	+	+

CASE 23: DISCHARGED ON 83RD DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th
Treatment:								
Penicillin								
Sulfadiazine								
Organisms:								
Staph., coag. +.....	+	+	+	+	+	+	+	+
Staph., coag. -.....		+						
Beta strep., group A.....		+						
Beta strep., other.....		+						
Alpha strep.....								
Gamma strep., aer.....	+							
Gamma strep., anaer.....								
E. coli, etc.....					+			
B. pyocyaneus.....	+	+	+					
B. proteus.....								
Cl. welchii.....	+	+	+	+	+	+	+	+
Other Clostridia.....	+	+	+	+	+	+	+	+
Diphtheroids.....	+	+	+	+	+	+	+	+
B. subtilis.....	+	+	+	+	+	+	+	+

when injected into the muscle of the thigh. Much less pain resulted when the 5,000 units of penicillin were dissolved in 1 cc.

Thirteen of the patients received penicillin at some time or other. One patient (Case 16) received the drug unintentionally for one day and the second (Case 29) received the drug during five days of a successful skin grafting late in the period of hospitalization. The remaining eleven patients received penicillin from the sixth to the fourteenth day or longer. The temperature response in these eleven patients is indicated in Table III. Accurate appraisal of the efficacy of the penicillin therapy is unfortunately impossible. The dosage employed is now known to have been too small

in light of subsequent observations by Dr. Keefer and ourselves. It was also given in the majority of the patients along with sulfadiazine. No toxic reactions were attributable to the penicillin.

Tables IV through XII summarize the bacteriologic findings in the patients with deep burns requiring skin grafting and treated with penicillin.

Table XIII summarizes the bacteriologic picture of the surface wounds. The initial contaminating flora was a mixture of staphylococci, alpha hemolytic streptococci, diphtheroids and *B. subtilis*. With the exception of the alpha hemolytic streptococcus these strains persisted as long as the wounds were unhealed. The group A beta hemolytic streptococcus was present initially in three patients and was subsequently implanted in three more patients. The secondary contamination occurred after the original strict

TABLE X
CASE 28: DISCHARGED ON 67TH DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
Treatment:									
Penicillin									
Sulfadiazine									
Organisms:									
Staph., coag. +.....	+	+	+	+	+		+	+	
Staph., coag. —.....	+	+	+	+					
Beta strep., group A.....									
Beta strep., other.....			+						
Alpha strep.....									
Gamma strep., aer.....	+								
Gamma strep., anaer.....									
<i>E. coli</i> , etc.....									
<i>B. pyocyaneus</i>									
<i>B. proteus</i>			+	+	+		+	+	
<i>Cl. welchii</i>									
Other Clostridia.....									
Diphtheroids.....	+	+	+	+			+	+	
<i>B. subtilis</i>	+	+	+	+	+				+

isolation was relaxed at the beginning of the third week. Anaerobic Clostridia were present initially but tended to disappear. A sufficient number of these anaerobes persisted to warrant immunization to tetanus. The most interesting finding was the distribution of the proteolytic gram-negative bacilli. *E. coli* was present initially in a few cases and tended to persist. *B. proteus* appeared at the end of the second week as the eschars of deep burns began to separate and was present in all unhealed wounds by the fifth week. *Pseudomonas aeruginosa* (*B. pyocyaneus*) was an inconstant contaminant.

INFERENCE FROM CLINICAL OBSERVATIONS

This program of treatment adequately controlled invasive infection. There was no evidence of cellulitis, lymphangitis, lymphadenitis or bacteremia. Superficial burns healed without suppuration in the usual 10- to 14-day period. The deep burns were all frankly infected and suppurative, but there was no evidence of marginal ulceration of healthy tissue. The outstanding feature of the infection was its limitation to the tissue devitalized by the original thermal injury. Pus formation was associated with the separation of the burn eschar and the presence of proteolytic gram-negative

INFECTION AND CHEMOTHERAPY

During this phase of slough local dressings of saline compresses were applied and the process of separation was hastened by bloodless surgical excision of the burn eschar. On the other hand, the decision as long as the wounds remained unhealed. Fever, leukocytosis, and positive cultures from the wounds were observed for skin grafting was based more upon the clinical appraisal of the wound

CASE 29: DISCHARGED ON 40TH DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th
Treatment:					
Penicillin					
Sulfadiazine					
Organisms:					
Staph., coag. +.....	+				
Staph., coag. -.....	+	+			
Beta strep., group A.....			+		
Beta strep., other.....			+	+	
Alpha strep.....					+
Gamma strep., aer.....					+
Gamma strep., anaer.....					
E. coli, etc.....					
B. pyocyaneus.....					
B. proteus.....					
Cl. welchii.....	+				+
Other Clostridia.....					
Diphtheroids.....			+	+	
B. subtilis.....	+	+	+	+	+

CASE 36: DISCHARGED ON 58TH DAY. REQUIRED SKIN GRAFTING

Weeks.....	1st	2nd	3rd	4th	5th
Treatment:					
Penicillin					
Sulfadiazine					
Organisms:					
Staph., coag. +.....	+				
Staph., coag. -.....	+	+			
Beta strep., group A.....	+				
Beta strep., other.....		+		+	
Alpha strep.....			+		
Gamma strep., aer.....			+	+	
Gamma strep., anaer.....					
E. coli, etc.....			+		
B. pyocyaneus.....	+				
B. proteus.....		+			
Cl. welchii.....	+		+		
Other Clostridia.....				+	
Diphtheroids.....	+				
B. subtilis.....	+	+	+	+	+

and the nutritional status of the patient than upon the bacteria present in the wound.

In summary, it may be stated that the method of treatment confined the bacterial infection to the devitalized tissue and protected the living cells from invasive infection or marked local necrosis.

DISCUSSION.—The inability to accurately identify the depth of thermal injury in the immediate posttraumatic period of observation is a serious handicap in the final evaluation of any method of treatment. It may be impossible to distinguish between a deep burn and an infected superficial

burn by an examination of the wound prior to skin grafting. Our experience indicates that a superficial burn heals kindly with any method of treatment that prevents destructive hemolytic streptococcal infection. It is equally true that no method of treatment has arrested the growth of bacteria in the deeply burned tissues. The treatment adopted in this group of cases was based upon the premise that the preservation of the vitality of the undamaged cells was a realistic objective in the treatment of burns. It is believed that reasonable success attended the use of a nonadherent occlusive local dressing and systemic supportive and antibacterial therapy. The failure to sterilize the devitalized burned tissue by such a method was not unexpected.

TABLE XIII

SUMMARY OF BACTERIOLOGIC FINDINGS

Weeks.....	1st	2nd	3rd	4th	5th	6th	7th	8th	9th
No. of cultures.....	24	17	10	9	9	5	6	4	1
Organisms:									
Staph., coag. +.....	20	16	9	8	7	5	5	3	1
Staph., coag. —.....	15	10	6	3	3	3	4	1	
Beta strep., group A.....	3	4	3	2	1		1		
Beta strep., other.....	1		3						1
Alpha strep.....	15	5	1	2		1			
Gamma strep., aer.....	1	1	1	1	2	2			
Gamma strep., anaer.....		1			1				
<i>E. coli</i> , etc.....	5	4	4	2			1		
<i>B. pyocyaneus</i>	1	1	3	2		3	1	1	
<i>B. proteus</i>	2	1	4	6	9	3	5	2	
<i>Cl. welchii</i>	6	2	1	1					
Other Clostridia.....	2			1	1	1	1		
Diphtheroids.....	17	15	10	8	5	5	6	3	1
<i>B. subtilis</i>	21	16	9	9	6	1	4	2	

Indeed, if it is ever possible to sterilize such tissue, the removal of the eschar may become a major problem.

The observation of this group of patients with controlled and limited infection has thrown into sharp contrast the derangement of bodily homeostasis incident to the traumatic insult of a major burn. This damage plus the metabolic burden of infection depletes the nutritional reserves and retards the convalescence of the patient. Resistance to infection and tissue repair are intimately correlated with recovery from this phase of negative balance.

CONCLUSIONS

The problem of preventing infection in burns has three components: Prevention of further contamination of wounds; effective antibacterial therapy for established contamination; and supportive measures to maintain the reparative and convalescent capacities of the patient.

REFERENCES

- 1 Jones, M., Holmes, L. F., and Hale, W. M.: Relative Efficiency of Aerobic and Anaerobic Methods in the Isolation of *Beta* Hemolytic Streptococci. *J. Bact.*, **42**, 138, July, 1941.
- 2 Todd, E. W.: Lethal Toxins of Hemolytic Streptococci and their Antibodies. *Brit. J. Exp. Path.*, **19**, 367, December, 1938.
- 3 Acutin, M. N.: *Trans. Kubyshev Milit. Med. Acad. Red Army*, **2**, 3, 1940.
- 4 Stewart, J. D.: Postoperative Shock Due to Hemolytic Streptococcus Wound Infection. *Surgery*, **9**, 204, February, 1941.

PROCEDURES IN REHABILITATION OF THE SEVERELY BURNED

BRADFORD CANNON, M.D.

FROM THE DEPARTMENT OF SURGERY, HARVARD MEDICAL SCHOOL, AND THE SURGICAL SERVICES,
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

FOURTEEN of the 39 patients admitted on the night of the disaster remained in the hospital after the special casualty ward was discontinued on December 13. Ten of these patients had third degree burns of sufficient extent to require further treatment. Only one of the ten was hospitalized for as long as 18 weeks. The average stay of the others was ten weeks, the minimum was three and one-half weeks and the maximum fourteen and one-half. During this time, one or more skin grafting operations have been performed on nine of the ten patients. The tenth patient had a small area of deep burn on the back which rapidly healed from the margins without grafting.

Distribution of Third Degree Burns.—The skin on the dorsum of the hand was the surface most frequently destroyed by third degree burn (fifteen hands in nine cases [Cases 2, 8, 11, 13, 20, 23, 28, 29 and 36], with both hands in six.) The arms were the next most frequently involved surfaces (ten arms in six cases [Cases 2, 8, 11, 13, 20 and 28], both being involved in four). The back was deeply burned in six patients (Cases 1, 8, 11, 13, 20 and 28), and the scalp and forehead in four (Cases 2, 8, 13 and 29). In three cases (Cases 2, 11, and 13) the legs were deeply burned, and in one of these (Case 13) the third degree burns extended almost completely around both lower legs and the lower third of both thighs. Scattered areas of the neck were deeply burned in Cases 8, 13, 20, 23 and 36.

Because of the similarity in distribution of most of these burns, it is interesting to speculate about the position taken by the victims as the fire spread rapidly across the ceiling. The hands were held protectively over the face, and the faces were deeply burned in only two cases. In one of these (Case 8) there were three vertical linear areas of third degree burn on the forehead. It appears that the forehead was burned between the separated protecting fingers. The extensor surfaces of the forearm and the lateral surfaces of the upper arm and shoulder were deeply burned in two cases (Cases 8 and 20), both women in evening dresses, who exposed these surfaces as the hands were held over the face for protection. Both of these women were burned on the back and in both the pattern of the underwear is evident (color section Fig. 12 a). It appears that the victims leaned forward and turned away from the most intense heat and were thus severely burned on the back, as well as on the arms and hands.

Treatment of the Local Wound.—The primary occlusive dressing of a fine-mesh gauze lightly impregnated with boric acid ointment* and applied with firm pressure has already been described (color section Fig. 15 a). Similar

* Boric acid ointment, 10 per cent, in petrolatum.

dressings were used after the first were changed between the fifth and tenth days. By the tenth to twelfth day the destroyed skin had begun to separate and there was suppuration about the margins with pus escaping through openings in the slough. No cellulitis or lymphangitis indicative of invasive infection was apparent. In order to insure better drainage of the wounds, constant wet dressings, with a single layer of fine-mesh gauze against the granulations, were applied at this time. These were kept moist by instilling 2 per cent boric acid solution through Dakin's tubes incorporated in the dressing. They were changed every second or third day. An alternation of wet and boric ointment dressings was tried, but because of the discomfort of the latter, especially on the hands, the wet dressings were continued until the time of grafting. The Bunyan envelope was used for several days in four patients (Cases 2, 11, 28 and 29) who had burns of the hands and forearms. The patients found them uncomfortable. The common complaint was of the humidity of the atmosphere when the bag was filled with oxygen and the burning pain when filled with normal saline. The absence of support for the hand and discomfort on contact of the hand with the envelope were also commented upon. Strands of slough and exudate were suspended in the water but did not separate. However, no hypochlorite was used, as Bunyan recommends.

Separation of Slough.—The average time before complete separation of the slough was twenty-five days. The maximum was thirty-six days, and the minimum sixteen days. This average interval is longer than one normally expects the process to take. There appears to be no correlation between the patient's general condition, the duration of chemotherapy, the extent of the burns, and this delayed separation. The relative freedom of the wounds from invasive infection may be of significance, as there was little pus beneath the slough when it was finally removed. Scattered islands of viable skin, 1 to 2 cm. in diameter, remained on the backs of some of the hands and arms after separation of the slough (color section Fig. 16 d). These had not been destroyed secondarily by infection.

Splinting of Hands.—An effort was made to hold the hands in the position of function but this could not be continued because of the pain. Flexing of the fingers put the open wounds on the dorsum under tension, and the patients could not tolerate it. Flexion also caused blanching of the granulations or skin over the metacarpophalangeal and interphalangeal joints, which increased the danger of further necrosis of tissue and possible exposure of the extensor tendons and the joints. Therefore, the fingers were allowed to remain in extension and the wrist in a neutral or slightly dorsiflexed position. This position was maintained until operation, at which time the hand and fingers were splinted in a more nearly normal functional position.

Preparation for Grafting.—After the special casualty ward was discontinued all dressings were done in an operating room set aside for these cases. The use of wet dressings applied with moderate pressure was continued after the slough had separated. The exposure of the raw surface,

COLOR SECTION

Containing 16 figures (49 subjects) in color to which reference has been made in several papers throughout the Symposium. The figures are numbered in this section in their own series, 1-16 a, b, c, etc. Corresponding text citations specify their appearance in this group.

SYMPOSIUM

ON THE

MANAGEMENT OF THE COCOANUT GROVE BURNS AT
THE MASSACHUSETTS GENERAL HOSPITAL

ANNALS OF SURGERY

JUNE, 1943

J. B. LIPPINCOTT COMPANY
Philadelphia, Pa.

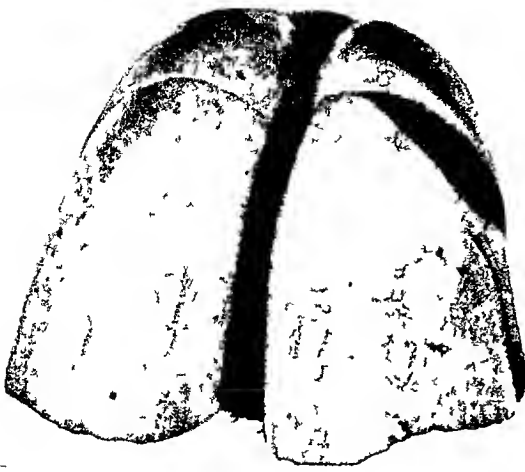


FIG. 1.—Lungs of case dead on arrival: The arresting feature is the bright pink color, attributable to carbon monoxide. An occasional subpleural hemorrhage can be seen. They are uniformly distended

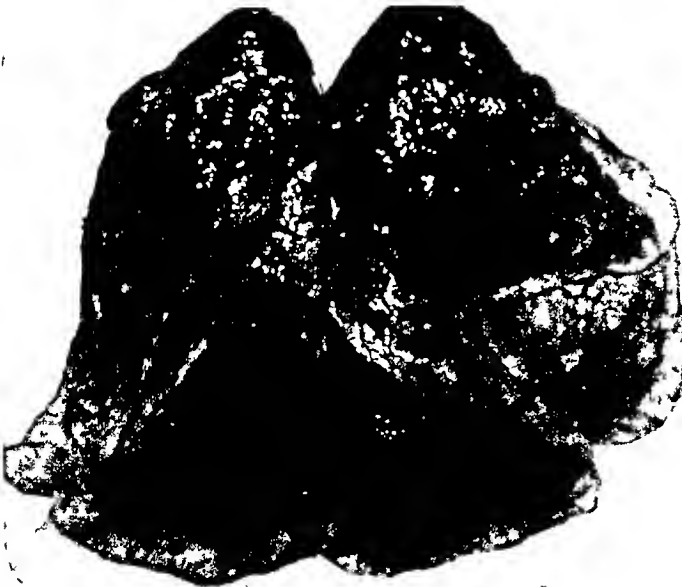


FIG. 2.—Lungs of Case 25: They are voluminous due to extensive anatomic emphysema. The posterior and central portions are deeply congested where the tissue can be seen through the dense anthracosis. Around the margins of all lobes is a light-colored zone two to four lobules wide in which air is trapped by the diffuse bronchostenos.

FIG. 3.—Larynx of Case 25 viewed from above: There is almost complete stenosis resulting from extreme edema of the mucous membrane and from fibrinopurulent exudate overlying the true and false cords.



FIG. 4.—Trachea of Case 25: There is a thick pseudodiphtheritic membrane extending downward from the larynx. After a short gap which is comparatively uninvolved it begins again in spotty form in the lower half of the trachea, where a few bits of black carbonaceous material are embedded in it. The mucous membranes are everywhere intensely injected, with scattered petechial hemorrhages.



FIG. 5.—Larynx and trachea from Case 7: The true and false cords are both markedly swollen and edematous. Beneath the cords is a black adherent membrane. Intense congestion and focal hemorrhages of the mucous membranes are apparent. There is a shallow ulcer just above the mouth of the right primary bronchus. The tracheotomy wound is scarcely visible, having been compressed by sharply folding back the cartilaginous rings.



FIG. 6.—A segment of the bronchial tree from Case 25: All mucous membranes are intensely red. In the secondary bronchi membranous bronchitis begins in spotty fashion. In the smaller bronchi the membrane becomes continuous and frequently occlusive. The pulmonary parenchyma is deeply congested and focally anthracotic.

FIG. 7.—Bronchial tree from Case 27: The mucous membranes are hemorrhagic and membrane formation is present though less pronounced than in Case 25. Clots protrude from the severed vessels which are, in part, antemortem. The parenchyma shows alteration of aeration and atelectasis.

FIG. 6.

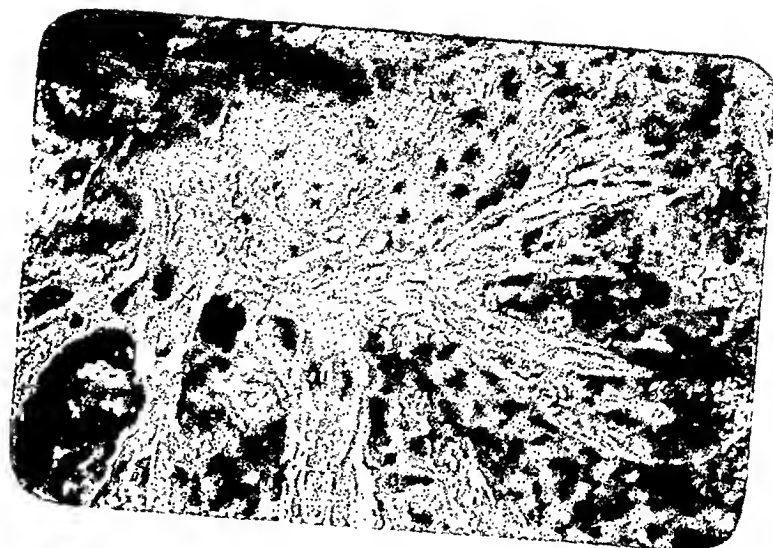


FIG. 7.

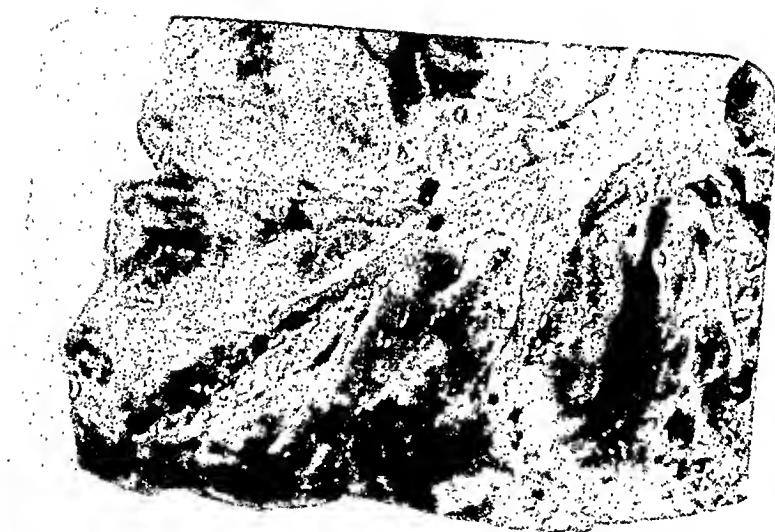


FIG. 8.—Posterior view of the lungs of Case 27: The basal portions of both lower lobes are massively atelectatic, dark red in color, depressed in contrast to the aerated parenchyma. Narrow prolongations of the atelectatic zone extend upward to the apices of the lobes. Another atelectatic zone can be seen on the lower margin of the left upper lobe.

FIG. 9.—Sagittal section of lung of Case 27: Membrane formation is visible in the secondary bronchi. A wide zone of dark, depressed, atelectatic tissue occupies the central part of the lower lobe. Aerated tissue is present above and below the area. The portion of upper lobe visible is all aerated.

FIG. 8

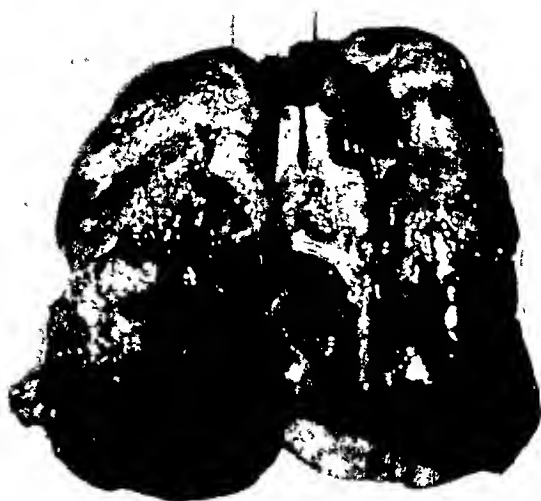


FIG. 9



FIG. 10.—View of the temporary operating room during the initial change of dressing on Case 20 on the seventh day. Surgeon is reapplying boric strips to face. Patient has had a tracheotomy. The dressings on the deep burns of the arms and hands are typical. (Note bacteriologist in right background and the photographer.)

FIG. 11 a and b. Case 13.—Appearance of circular burns of legs on tenth day. This was the most severely burned patient who survived. She also had deep burns of the hands and arms, scalp, forehead, and back; total extent of second and third degree was 56 per cent. Note the dry slough above the right knee and the moist slough immediately adjacent on the lateral aspect of the thigh.

FIG. 11 c. Case 13.—Legs on the 33rd day after all the slough has separated. The surface is pale and the underlying fat is visible. No granulation tissue has appeared.

FIG. 11 d. Case 13.—Legs on 64th day. A thin layer of granulation tissue has developed. There is wasting of both legs resulting from the debilitating effect of chronic sepsis in the open wounds. Contracture of right tendo achillis is present.

FIG. 11 e. Case 13.—Legs on 71st day. A striking change has occurred; there has been a rapid advance of epithelium from the margins and the granulation tissue now has a healthy appearance. This change is attributable to the improvement in the patient's general condition from intravenous feeding and repeated transfusions.

FIG. 11 f. Case 13.—Legs on 81st day, tenth day after grafting. There is a complete take of the grafts. The small unhealed areas were not covered at the operation.

FIG. 11 g. Case 13.—Legs on 91st day. Healing is practically complete.

FIG. 12 a. Case 8.—Deep burns of the back at the time of the first change of dressing on the fifth day. The outline left by the clothing is visible. Note the dressings covering the deep burns of the arms. This patient also had second and third degree burns of the head, neck, arms, hands and legs; total extent 29.1 per cent.

FIG. 12 b. Case 8.—Back on the tenth day. The slough has begun to dry. There is exudate about the margins but minimal evidence of inflammation in the adjacent skin.

FIG. 10



FIG. 11 a



FIG. 11 b



FIG. 11 c



FIG. 11 d



FIG. 11 e



FIG. 11 f



FIG. 11 g



FIG. 12 a



FIG. 12 b



FIG. 12 c. Case 8.—Back on the 12th day. Separation of the slough has started, exposing a thin exudate over the viable underlying tissue. No abscesses or other evidence of destructive infection were encountered.

FIG. 12 d. Case 8.—Back on the 19th day. The slough has separated but there is still some exudate adherent to the raw surface.

FIG. 12 e. Case 8.—Back on the 31st day. The granulations are now clean and healing has begun.

FIG. 12 f. Case 8.—Back on the 64th day, practically healed. No skin grafts were applied. Twenty-five days before this photograph was taken, the arms and hands were grafted.

FIG. 12 g. Case 8.—At four months keloid has appeared in the burned areas of the back. Patient is troubled with moderate itching.

FIG. 13 a. Case 2.—Right hand at the time of the first change of dressing on the fifth day. This is a second degree burn and edema is still present. Patient also had second or third degree burns of the left hand, wrist, face, scalp, thighs and legs; total extent 17.5 per cent. (See Figures 14 a through j.)

FIG. 13 b. Case 2.—Right hand on ninth day. The edema is subsiding and there is no evidence of infection.

FIG. 13 c. Case 2.—Right hand on 13th day. Epithelization is taking place rapidly from undestroyed cells in the deeper layers of the skin.

FIG. 13 d. Case 2.—Right hand on 19th day. Further healing has taken place.

FIG. 13 e. Case 2.—Right hand on 26th day, healed. For final result see Figure 14 j.

FIG. 12 c



FIG. 12 d



FIG. 12 e



FIG. 12 f



FIG. 12 g



FIG. 13 a



FIG. 13 b

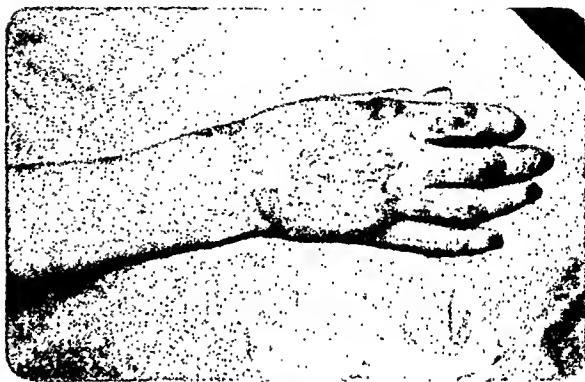


FIG. 13 c



FIG. 13 d



FIG. 13 e



FIG. 14 a. Case 2.—The left hand at the time of the first change of dressing on the fifth day. The outlines of the third degree burn are already apparent. The damaged superficial skin of the fingers and thumb has not been removed. There is slight edema of the hand.

FIG. 14 b. Case 2.—Left hand on ninth day. The slough has begun to separate. Although bacteria have been recovered on culture, there is minimal infection.

FIG. 14 c. Case 2.—Left hand on 13th day. More slough has separated.

FIG. 14 d. Case 2.—Left hand on 19th day. The slough on the wrist was removed mechanically; that on the dorsum of the hand is still adherent. The surrounding skin is uninfected.

FIG. 14 e. Case 2.—Left hand on 26th day. The slough has been removed. The extensor tendons of the index and middle fingers are exposed over the metacarpophalangeal joints. Exudate is still adherent to the granulations.

FIG. 14 f. Case 2.—Left hand on 28th day. Absence of invasive infection permits insertion of hand into abdominal wall pocket in an effort to preserve the exposed tendons. Note the decrease in exudate overlying the granulations in past two days.

FIG. 14 g. Case 2.—Left hand on 28th day; is in the pocket and the raw surface on the wrist has been covered with split graft.

FIG. 14 h. Case 2.—Left hand in pocket on 33rd day, five days after insertion. Absence of virulent infection of hand is demonstrated by paucity of inflammation of pocket walls. There is a narrow zone of cellulitis about the opening through which the index finger emerges.

FIG. 14 i. Case 2.—Left hand on 48th day, detached, 20 days after insertion. The color of the flap is good and the edges have been sutured in place. (The nail polish has been present since the night of the fire)

FIG. 14 j. Case 2.—Appearance of hands at four months. The tendons have been preserved and function is returning. The fullness of the flap is diminishing but some fat may have to be excised later.

FIG. 14 a



FIG. 14 b



FIG. 14 c



FIG. 14 d



FIG. 14 e



FIG. 14 f



FIG. 14 g



FIG. 14 h



FIG. 14 i



FIG. 14 j



FIG. 15 a. Case 29.—Second degree burns of face and ears and third degree of scalp covered by the primary occlusive dressing which was applied on the night of admission. Only the mouth and nares are exposed but patient can breathe comfortably. Patient also had second and third degree burns of hands and arms, total extent 12.5 per cent.

FIG. 15 b. Case 29.—View of the neck and chest on the third day showing the massive subcutaneous edema in these unburned areas. This edema fluid was expressed from the burns of the face and scalp by the pressure dressing and gravitated downward.

FIG. 15 c. Case 29.—At the time of the first change of head dressing on the seventh day. There is edema of the face in spite of the pressure dressing. The remnants of destroyed skin and dry serum are still present and uninfected.

FIG. 15 d. Case 29.—Face on ninth day. The edema has diminished. There is still weeping from the skin and crusts have reformed. Some skin debris is still present.

FIG. 15 e. Case 29.—Final view of face on the 55th day showing the absence of scarring and return to normal contours. Scalp healed without grafting; (hands and arms were grafted).

FIG. 16 a. Case 28.—View of the left hand and arm at the time of the first change of dressing on the fifth day. Note the unruptured blebs on the arm and the remnants of destroyed skin on the wrist and fingers. There is no evidence of infection in these wounds. The fluid removed from the bleb is sterile and the sulfadiazine level in this fluid is 6.7 mg. per cent (that of the blood 6.6 mg. per cent). Patient also had second degree burns of face, neck, back, right hand and arm; third degree of back; total extent 24.5 per cent.

FIG. 16 b. Case 28.—Left hand and forearm on 19th day. Slough is still in place. The skin immediately adjacent is normal in appearance without evidence of infection.

FIG. 16 c. Case 28.—Left hand and forearm on 30th day. Most of the slough has separated. The granulations are edematous. Infection is minimal.

FIG. 16 d. Case 28.—Appearance of the hand and forearm on the 51st day, the day of grafting. Note the healthy appearance of the granulations and the islands of viable skin in the center of the raw surface on the back of the hand.

FIG. 16 e. Case 28.—Final view of the hands at three and one-half months.

FIG. 15 a



FIG. 15 b



FIG. 15 c



FIG. 15 d



FIG. 15 e



FIG. 16 a



FIG. 16 b



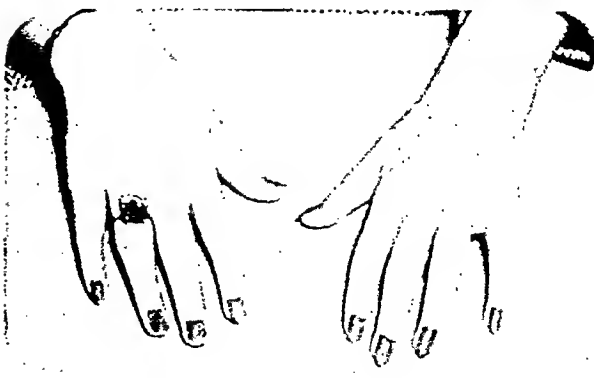
FIG. 16 c



FIG. 16 d



FIG. 16 e



REHABILITATION OF BURN CASES

especially of the hands, was painful, and in some cases nitrous oxide-oxygen anesthesia was given to help the patient's morale by eliminating the pain and to reduce the time taken for the procedure. The wet dressings acted as a keratinizing stimulus, particularly on the areas of second degree burn adjacent to the granulations and on the advancing marginal epithelial surfaces. This débris did not develop when an ointment dressing was applied. The débris, which became macerated, grew staphylococci and saprophytes on culture. At each change of dressing the surfaces were carefully cleaned with soap and water to reduce as much as possible this source of contamination of the wounds. The persistence of infection and edema of the granulations after the slough had separated may be attributed in part to this maceration. In most of the cases general chemotherapy had been discontinued before the time of grafting. Oral sulfadiazine was given to Cases 8 and 13 both pre- and postoperatively, and to Case 29 for the first operation. Penicillin was being given intramuscularly to Cases 2, 20, 29 and 36 at the time of their first operations but was discontinued a few days later. All other operative procedures were undertaken without general chemotherapy. Local sulfanilamide powder, in controlled doses, was dusted on the raw surfaces preoperatively in several cases. The edema subsided and the drainage decreased with this treatment more rapidly than with the wet dressings alone. There were no losses of the graft following the local use of sulfanilamide.

All patients were given a high protein and high vitamin diet throughout the hospital stay. In Case 13, because of inadequate mouth intake, it was necessary to feed by stomach tube with supplementary daily intravenous amogen, glucose, and vitamins. Anemia was controlled by repeated whole blood transfusions. A total of twenty-five were given. Two weeks after this intravenous therapy was started, the patient's general condition and the condition of the local wounds had improved so much (color section Fig. 11 e) that both legs were grafted. The grafts took completely.

OPERATIVE PROCEDURES

Anesthesia.—Ether anesthesia was used in 13 of the 21 operations. Spinal anesthesia was administered for all operations on Case 2, and was supplemented with sodium pentothal at the first operation and brachial block at the third. Local infiltration was used in Case 29, and spinal in Case 36, when cutting the grafts. No anesthesia was used when applying the grafts to the hands in these two cases. The other operation upon Case 29 was performed with sodium pentothal anesthesia, and one of those on Case 13 with spinal. There were no complications from anesthesia in any of the patients who had lung damage.

Grafting.—Split-thickness grafts* were used for covering the raw surfaces with the exception of the back of the hand of Case 2, which was covered by a direct abdominal flap (color section Fig. 14 a-j). Undamaged extensor

* The donor areas of the grafts were dressed with a fine-mesh gauze lightly impregnated with scarlet red ointment. The overlying gauze sponges were held in

tendons of the index and middle fingers of this hand were exposed over the metacarpophalangeal joints for a distance of 3 to 4 cm. The granulating surface extended from the wrist to the proximal phalanges of the two fingers and involved most of the back of the hand. In order to save these tendons from destruction by infection and to insure normal function in the future, a flap

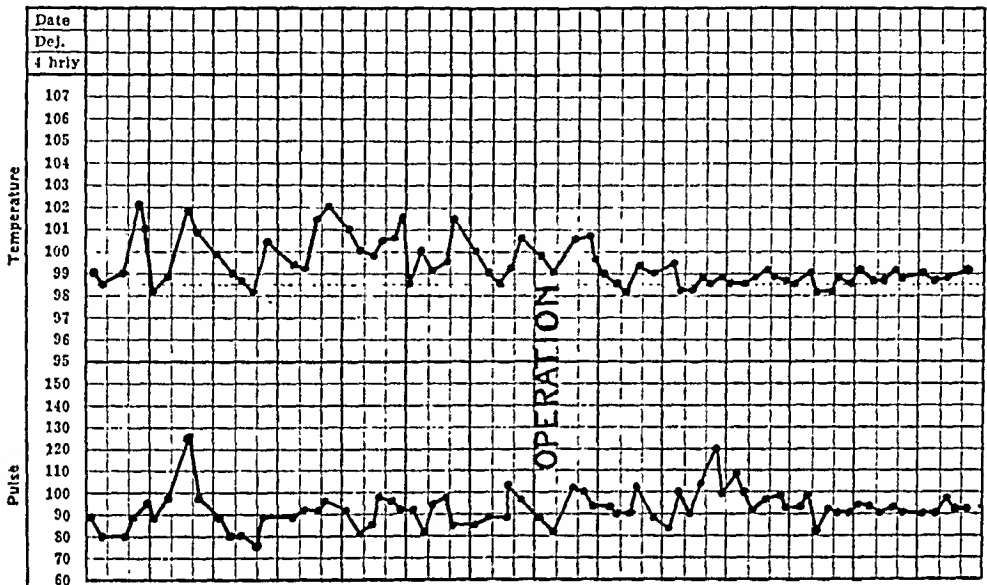


FIG. 41.—Chart of Case 8 at the time of operation on the thirty-ninth day. The preoperative temperature and pulse curves resemble those of all the patients who had large, granulating, surface wounds. Note the prompt descent of the curves to normal after the raw surfaces were covered with skin grafts.

was used instead of a free graft. The operation was performed on the twenty-eighth day. There was little surface infection and culture grew only coagulase-positive staphylococcus and *B. proteus*. The raw surface was gently cleansed with soap and water, but the granulations were not disturbed. A pocket was made in the abdominal wall with a large opening laterally, through which the hand was inserted, and with smaller openings, through which the thumb and fingers emerged. A small raw surface just above the wrist was covered by a split-graft at the same time. The arm was immobilized by adhesive strapping. One border of the flap was severed on the fourteenth postoperative day, and the hand detached on the twentieth day. Three weeks later the defect on the abdominal wall was grafted.

A total of 17 grafting operations were performed on the other eight patients (Fig. 41). The first graft was applied on the twenty-third day to the back of the hand of Case 29, and the last at four months to several small areas on Case 13. Case 36 was grafted on the twenty-fourth day. Six operations were performed during the sixth week (Cases 8, 11, 20, 23, 29 and 36). Two were done in the eighth (Cases 23 and 28). One was performed in the ninth (Case 13). Two were performed in the tenth

place with cotton or ace bandage. When the grafts were taken from the thighs the whole leg was wrapped in an encircling ace bandage. All dressings were removed between the twelfth and fourteenth day unless small unhealed areas were discovered.

REHABILITATION OF BURN CASES

(Cases 20 and 23). Two were performed in the thirteenth (Cases 11 and 13). And, subsequently, two minor procedures have been undertaken on Case 13.*

At operation, the raw surfaces were prepared with soap and water. The granulations and the narrow zone of skin that had grown in about the margin were shaved off in all cases, except on the hands of Cases 29 and 36. There was a moderate loss of blood in this procedure, but the graft acted as an efficient hemostatic agent, and a smooth, firm base for it was secured. Most of the grafts were sutured accurately in place, but, where possible, a carefully applied dressing gave adequate anchorage and sutures were not used. The grafts were perforated only if oozing persisted beneath them.

All postoperative dressings were applied wet and kept wet by irrigation through Dakin's tubes. A single layer of fine-mesh gauze was used against the graft, and the overlying dressing consisted of sponges and a thick layer of mechanic's waste held firmly in place with cotton bandages. Sterile, well-padded wood splints were used to immobilize the hands and arms after operation. A bulky dressing was sufficient for fixing the ankles and feet but padded wood splints were used at the knees. The first dressing was done on the fifth or sixth day after operation. Boric ointment gauze was applied in all cases. Subsequent dressings were done on alternate days as long as was necessary.

All the grafts were successful except those on Cases 23 and 36. Both hands were grafted in each of these patients. Operation upon Case 23 was performed on the thirty-seventh day, and on Case 36 on the twenty-fourth day. On the second postoperative day Case 23 had a plasma protein level of 5.5 mg. per cent, and a hematocrit of 24 per cent, for which two 500 cc. transfusions were given. Cultures at the time of grafting, from the left hand showed *Staphylococcus albus*, coagulase-negative, and *B. proteus*. From the right hand was grown hemolytic *Staphylococcus aureus*, coagulase-positive, *beta* hemolytic streptococci, *B. proteus* and diphtheroids. Five days before operation in Case 36 the plasma protein was 8.1 per cent, and the hematocrit 44 per cent. Cultures of the hands at operation grew hemolytic *Staphylococcus aureus*, coagulase-positive, *beta* hemolytic streptococcus and several saprophytes. Case 23 is the only one showing a significant variation from normal plasma protein and hematocrit at the time of operation, and these patients are the only ones having a positive culture of *beta* hemolytic streptococcus from the granulating surfaces. Case 23 was operated upon twice at biweekly intervals before the hands were completely healed. Sulfanilamide powder was used locally before the second of these operations. Case 36 was grafted again 11 days after his first operation.

* Case 13 received a sternal transfusion on the sixth day. There was extravasation of the blood into the tissues of the chest wall and the breasts. Subsequently localized tenderness, heat, and a bronzed discoloration of the overlying skin developed. A large abscess was drained on the twelfth day. Twenty-one days later a revision of the wound was necessary to give better drainage. The resulting defect, which measured about 12 cm. in diameter, was later grafted.

PROGRESS AND RESULTS

The burns of the extremities, especially the hands, were the first surfaces grafted for reasons of comfort and early restoration of function. The relatively small areas of third degree burn on the faces were grafted as early as possible for cosmetic reasons.

Fingers.—On many of the fingers there was a narrow zone of third degree burn on the dorsal surface. Healing occurred rapidly in the two distal phalanges but grafts were necessary for covering the proximal phalanx in fingers of Cases 8, 11, 20, 23, 28 and 36. The extensor tendon of the index and little fingers of the left hand were exposed over the proximal interphalangeal joints in Case 8. Healing is complete but there is absence of full extension at these joints. In Case 20 the proximal interphalangeal joint of the left index finger was exposed and has remained open. There is adequate soft tissue drainage, and ultimately sequestration of bone and destruction of the joint is anticipated. For cosmetic reasons the finger is splinted in extension. Case 13 had these same joints exposed in all four fingers. The fingers have been held in extension with a banjo-splint, and healing has taken place without sequestration. The four fingers of the right hand were so badly burned that only the palmar skin remained viable. Amputation was performed distal to the metacarpophalangeal joints on the thirty-third day. This patient also had a localized deep burn over the lateral aspect of the thenar eminence, with destruction of the underlying muscle and exposure of the metacarpal bone. Spontaneous healing took place following débridement and free drainage.

There has been minimal thickening of the skin on the fingers and no true keloiding in any of the cases.

Hands.—One or both hands of Cases 8, 11, 13, 20, 23, 28, 29 and 36 were grafted. Most, or all, of the dorsal surface of these hands had to be covered (color section Fig. 16 a-e). In a few of the cases epithelium from early spontaneous healing was not excised at operation and there is now a poor bearing surface easily broken by trauma. In Case 2, who had the direct abdominal flap, the tendons were salvaged, and there is normal extensor function. A thick layer of abdominal fat is present in the flap, giving a bulky appearance. This excess fat will be excised at a later date for cosmetic reasons (color section Fig. 14 a-j).

There has been some thickening of the scars at the margins of the grafts, and true keloids have developed on the backs of the hands of Cases 21 and 36. These were the two patients in whom there was loss of the grafts and in whom secondary operations were performed. Because of the scarring, the back of the hand is tight and flexion of the fingers and hand tenses the skin of the forearm. Further corrective procedures will have to be undertaken in these cases.

Arms.—The arms of Cases 8, 11, 20, and 28 were all grafted successfully. Good covering was obtained and there has been good recovery of function without contracture. No keloid has developed.

REHABILITATION OF BURN CASES

Back.—Although the backs of Cases 1, 8, 11, 13, 20 and 28 had third degree burns of varied extent, only that of Case 11 was grafted. After the slough was removed, healthy granulations appeared and spontaneous epithelization occurred quite rapidly. In the meantime, all except Case 1 were being treated for deep burns of the extremities. During this period the patients lay on their backs with very little discomfort.

In the central areas, which were the last to heal, there is keloid developing. This change has not appeared in the marginal surfaces of spontaneous healing, which lie nearer the normal skin. No keloiding has occurred in the areas grafted on Case 11. Only Cases 8, 11 and 28 have complained of itching of the back, but these had extensive burns (color section Fig. 12 a-f).

Forehead and Scalp.—Case 8 had a third degree burn of the forehead which was grafted. Cases 2 and 29 had burns of the scalp which were small and healed without grafting. Case 13 had a third degree burn of all the forehead and right temple which extended posteriorly in the left parietal region to an area about 12 cm. in diameter over the occiput. In the center of both the forehead and the occiput, bare bone was exposed. A 4 cm. disk of outer table of posterior skull has separated spontaneously, but a small area of bone is still exposed on the forehead. All of the granulating surfaces have been grafted successfully. No keloiding has developed in these areas.

Ears.—In Case 13 there was a deep burn of the ear with exposure of cartilage at the rim of the helix. Healing took place when adequate soft tissue drainage was established and minimal loss of cartilage occurred.

Neck.—Case 13 had a linear third degree burn of the left side of the neck which healed without grafting, but there is a moderate contracture. In Cases 8, 20, 23 and 36 there were narrow bands of deep burn which caused no contracture but which have begun to keloid.

Legs.—Of the three patients (Cases 2, 11, and 13) who had deep burns of the legs, only two (Cases 11 and 13) were grafted. They are now healed. Case 13 had extensive raw surfaces which were grafted at four months; there are no contractures but a moderate shortening of the right Achilles tendon has developed; no keloid has appeared (color section Fig. 11 a-g).

COMMENT

The protection of all tissue cells not destroyed by the heat is the ultimate purpose of any method useful in the local treatment of burns. Because infection is a destructive process and because destructive organisms grow in traumatized tissue, it has been common practice, regardless of the surface agent applied, to débride all burns at the time of the definitive treatment. The evaluation of the unorthodox method employed in this group of patients depends on determining whether the healing time was prolonged because the burns were neither débrided nor cleansed before the first dressings were applied.

It is well known that uninfected second degree burned surfaces usually heal within two or three weeks. The same interval of healing was ob-

served in this group of patients. Examination of the wounds at the time of the first and subsequent dressings revealed a clean surface with no purulent exudate, cellulitis, or acute tenderness. The destroyed epithelial débris was dry and the contents of the intact blebs were sterile. Therefore, it is apparent that the failure to débride the wounds initially did not delay the healing of the second degree burns in any measurable degree.

In the smaller group of patients who had both second and third degree burns, the injured surfaces remained clean during the first two weeks, with minimal exudate and no cellulitis or acute tenderness. By the end of two weeks the areas of second degree burns were epithelized and uninfected, while in the immediately adjacent areas of third degree burn, slough was separating (color section Fig. 16 b). *Satphylococci* and the saprophytes grew in the slough but did not invade the living tissues. When removed, only a thin exudate was found beneath the slough with no abscesses. In the hand of Case 2 exposed tendons were found. These remained viable in the granulating wound and were salvaged by covering them with an abdominal flap on the 28th day (color section Fig. 14 a-j). It is apparent from these observations that the wounds were free from invasive infection and that there was no measurable delay in carrying out the reparative procedures.

It seems reasonable to conclude from these observations, both on the second and third degree burns, that débridement and cleansing need not be part of the treatment. Tissue resistance and general chemotherapy can be relied upon to prevent invasive infection. However, for success, an ointment gauze should be used to allow serous drainage into the overlying dressing. The surface must not be sealed by an impervious membrane or eschar. Precautions should be taken to reduce contamination by avoiding careless exposure of the wounds at the primary dressing and too frequent subsequent changes. For this reason and because all wounds in these cases remained so free from infection, the first change of dressing should probably be postponed for 12 to 14 days.

The importance of the general nutritional state in the spontaneous healing of burned surfaces and the preparation of these surfaces for successful skin grafting cannot be overemphasized. Only by early skin grafting can large burned areas be covered and the development of contractures be avoided.

A NOTE ON PHYSICAL THERAPY

ARTHUR L. WATKINS, M.D.

FROM THE DEPARTMENT OF PHYSICAL THERAPY AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

SIX PATIENTS who received severe burns to the dorsum of the hands and wrists were referred to the Physical Therapy Department either while in the hospital or at the time of discharge to be treated as out-patients (Cases 2, 8, 23, 28, 29 and 36). In all cases surface healing was complete before beginning treatment. The first patient (Case 29) was referred to this department 51 days after the fire, so that the maximum period of physical therapy at the time of writing was 70 days, three to five treatments being given each week. There are, of course, no end-results to be reported at this time, for continued improvement is anticipated for the next six to twelve months, or longer.

METHODS OF TREATMENT

As these patients were splinted in extension, the aim of physical therapy was to restore flexion in the digital joints and wrists also if involved. In the one case in which a direct abdominal flap was undertaken (Case 2) there was the additional problem of mobilizing the shoulder, which had developed an adduction-internal rotation contracture from the fixation required for this type of transplant.

During the first few weeks of treatment the grafts and newly epithelized areas were quite thin and sensitive to very minimal trauma whether mechanical or due to heat. Because of this, a layer of lanolin was gently applied over the new epithelium. The whirlpool bath, at a temperature of approximately 104° F., was then used for a period of 15 to 20 minutes. In some cases the initial bath temperature was slightly lower, later being increased as tolerance developed. While still in the bath the patients were instructed to start gentle, slow, steady active flexion of the fingers and wrists up to the point of discomfort. When sufficient flexion allowed, the patients were given rubber sponges to grasp, as a form of underwater exercise. After several weeks of the whirlpool bath, when the epidermis was stronger and thicker, the melted paraffin wax bath was substituted for it. The temperature in these baths was maintained at 126° F., and accordingly produced much greater and longer-lasting hyperemia and increased relaxation of tense structures. In addition, a thin film of oil remained after removal of the wax coating, which was an excellent lubricant for massage. Following this thermotherapy massage of a special type was given. This consisted of gentle circular and longitudinal friction at the junction of the normal and involved areas. The friction was not between the technician's fingers and the skin, but between the skin and subcutaneous layers and the underlying bone, tendons and muscles. By this method some loosening of

scar could be obtained without traumatizing the new skin. Massage was also given in such a way as to pull the normal skin in the direction of the knuckles in order to relax tension which was maximal at that point. Simultaneously with this stretching of normal skin the patient was instructed to actively flex the fingers as much as possible. Occasionally gentle passive stretching of the firmer bands of scar was done with one hand while massaging with the other. The intensity of this passive procedure, however, was very carefully regulated to avoid traumatizing the new skin.

Exercises followed massage and for the most part were active guided voluntary motions. Emphasis was placed on slow steady stretching to the point of discomfort and degree of skin tension thought advisable as judged by the blanching over the metacarpophalangeal and interphalangeal joints. In addition to intensity, the frequency of repetition of the exercises had to be regulated, both during treatments and at home. It was soon found that excessive movements lead to small blister formation in some patients and avoidance of this was an additional guide to dosage.

An important part of the therapeutic exercise program was teaching relaxation. These patients unconsciously had a tendency to hold the fingers in complete extension and protected the hands from all possible contacts. To overcome this habitual attitude which delayed return of function, they were constantly reminded to make use of their hands in a natural way for the numerous and frequently repeated movements usually pertaining to eating, dressing, gesticulating, *etc.* As the hand is such an intricate mechanical mechanism, actual use in tasks of appropriate degree of difficulty was further advised to increase function, rather than relying on set exercises alone. The occupational therapists were helpful on this score in suggesting and supervising practice work such as typewriting, knitting and light carpentry. Some of the patients took this lead as an incentive to carry on increasingly difficult manual maneuvers on their own initiative, such as developing and printing photographs and playing jackstones.

RESULTS

No true end-results are warranted at this date as the physical therapy for these patients has really just begun. It is possible, however, to demonstrate the rate of improvement in function as progress has been recorded by double exposure action photographs.

Case 36 was one of the first to receive physical therapy. Treatments started the sixty-second day, at which time there was only a jog of motion in the finger joints. Action photographs show approximately 50 per cent of normal joint motion 18 days after the first treatment (Fig. 42 A) and nearly complete flexion 35 days later after a total of 30 treatments (Fig 42 B).

Cases 2, 8, 23, 28 and 29 had the same type of physical therapy and have made comparable progress with the exceptions noted below.

COMMENT

The most striking feature, so far concerning return of function following

PHYSICAL THERAPY

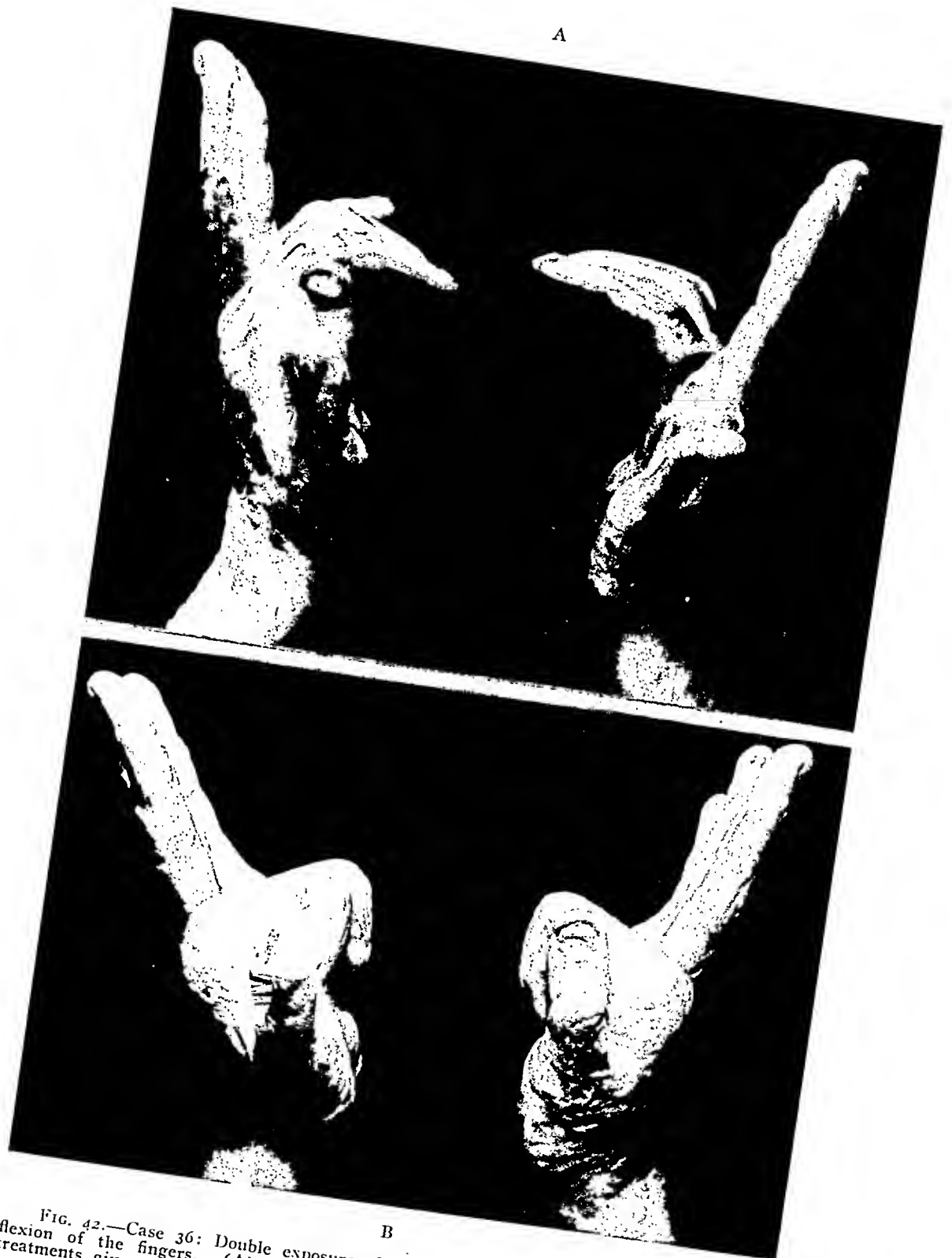


FIG. 42.—Case 36: Double exposure photographs to show maximum extension and flexion of the fingers. (A) February 5; (B) March 12. Thirty physical therapy treatments given starting January 29, 1943.

physical therapy, was the slowness and difficulty in regaining flexion of the metacarpophalangeal joints in certain cases in spite of good healing and take of the grafts. Analysis of these instances revealed that if the burned area extended beyond the dorsum of the hand and involved the wrist as well, finger flexion was always more limited. It does not appear likely that tendon involvement is responsible since wrist flexion was not limited proportionately. Normally flexion of the metacarpophalangeal joints results in distal movement of the skin over the wrist and hand as much as six to eight millimeters. Restriction of this skin movement which should start two to three centimeters proximal to the wrist is the probable mechanism of the prolonged finger disability.

The return of function already obtained in these patients under treatment for a relatively short period is encouraging. There appears to have been minimal permanent joint or tendon injury and the prognosis seems good for eventually securing excellent function of the hands.

THE PROBLEM OF BURN SHOCK COMPLICATED BY PULMONARY DAMAGE*

OLIVER COPE, M.D., AND FREDERIC W. RHINELANDER, M.D.

FROM THE DEPARTMENT OF SURGERY OF THE HARVARD MEDICAL SCHOOL AND THE SURGICAL SERVICES AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

The treatment of shock of the casualties demands priority in a disaster. Proper immediate shock therapy may prevent early death among burn casualties and also influence the future course because the fight against infection depends upon the patient's well-being.

The pulmonary lesions in the casualties of the Coconut Grove disaster were unexpected and complicated the care of the shock. The usual plan of action for the care of shock due to burns had to be promptly modified. Carbon monoxide poisoning with its bright cherry-red color of the burn surfaces and mucous membranes, and the inflammation of the burned lungs and airways were quickly detected, but there was a delay in recognizing that the resulting anoxia was the cause of the mania in some of the patients. Dr. Beecher, in his article, deals with the problems of anoxia. In this article we detail the modifications deemed necessary for the care of the burn shock.

A disaster close to hospital facilities offers the ideal circumstances for the care of shock. For the prevention of shock is more effective than its treatment when once it is established. This is particularly true of burn casualties where the shock, except for the primary phase due to pain and exposure, has a longer latent period than shock from hemorrhage. The Coconut Grove night club was sufficiently close to the Massachusetts General Hospital so that all the casualties arrived within two hours of the onset of the fire. The shock that had been suffered by the time of arrival was due not to burns so much as to the anoxia, exposure and pain. The steps taken in the treatment of shock were as follows:

Control of Pain.—Each patient immediately upon admission was given an injection of morphine. This procedure, routine in the treatment of burns, is based on the concept that prolonged pain in itself leads to shock. That a few of the patients received an overdosage from a mistaken idea of therapy is emphasized by Dr. Beecher.

That pain may exert an additional and indirect influence on shock is illustrated by Case 12, a young naval officer. One of the earliest patients to arrive, he walked in. There was a delay before he received the morphine. The pain in his hands was so intense that he was unable to lie down but jumped up and down on the floor waving his hands. Twenty-five hours later he died of the pulmonary complication. It is a question whether this initial excessive physical exertion may not have increased the pulmonary edema. It is a common belief as a result of experiences in the last war that exertion precipitates the onset of pulmonary symptoms and edema following phosgene inhalation.

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

General anesthesia was deliberately omitted as part of the treatment of the casualties since it has a deleterious influence in patients in impending shock. The surface treatment, with no débridement and no cleansing, was planned with this in mind.

Minimum of Manipulation.—Every effort was made to reduce manipulation in the care of the patient. Rolling a patient over abruptly tends to disturb the vascular equilibrium with which he is responding to the diminishing blood volume. But one shift of the patient was made, from stretcher to bed. All subsequent procedures were carried out in bed. Had débridement and cleansing been performed it would have necessitated a transfer of patient from bed to operating table and back, as well as the manipulation incident to the débridement.

Plasma Therapy.—All except ten of the patients were given plasma intravenously. Of those receiving no plasma, five had minor pulmonary complications and no surface burns, and were discharged from the hospital in the first few days (Cases 9, 10, 21, 30, and 31); the other five had minor surface burns and various degrees of pulmonary signs (Cases 1, 3, 5, 15, and 24). Because of the inevitable delay in the thawing of plasma in the blood bank, the early arrivals did not receive plasma promptly, whereas the later arrivals had plasma running into their veins within five minutes of entry. Plasma therapy was deliberately withheld from the patients with *early* signs of pulmonary damage and no, or minor, external burns. To one patient, (Case 6) with no external burn but severe pulmonary damage, one unit of plasma was given later in the night.

The initial dosage of plasma was determined on the basis of the surface area of the burns.* For each 10 per cent of the body surface involved, it was planned to give 500 cc. in the first 24 hours. Because the plasma delivered by the Blood Bank during the first 36 hours was diluted with an equal volume of physiologic saline solution, the patient was to receive 1000 cc. of fluid for each 10 per cent burned.

The plasma dosage was modified subsequently on the basis of repeated hematocrit and serum protein determinations. The hematocrit readings on blood taken in the third hour after entry were available by 3 A.M. of the first morning. The rate of plasma administration was increased in the patients showing hemoconcentration. Four additional blood hematocrit and protein determinations were made in the first 24 hours. Three determinations were made in the second 24 hours; two in the third; and daily thereafter as indicated. No attempt was made to apply a formula to the hematocrit reading to determine the dosage of plasma needed, it was simply run in faster when hemoconcentration was present. The same basic formula of surface area

* No attempt was made to judge the amount of plasma which might be lost from the circulation into the damaged pulmonary tissue. That the lungs accounted for some of the plasma lost is indicated by the fact that those lungs examined postmortem by Drs. Mallory and Brickley weighed nearly one kilogram more than an average pair of normal lungs.

SHOCK

was adhered to.* Only two patients (Cases 4 and 39) showed a hematocrit reading below normal in the first 24 hours.

The results of this intravenous plasma saline therapy were apparently satisfactory in the initial 12 hours. Although forms of shock certainly existed, little or no burn shock was encountered.† No patient died in the first 12 hours. (The unknown number who died immediately at the entrance from suffocation are excluded.) The seven deaths counted occurred from 13 to 62 hours after admission and all were considered to have been caused by pulmonary damage and anoxia.

Little or no hemoconcentration, as judged by the hematocrit and serum protein, occurred in the patients with the most extensive surface burns. For example, in three of these patients (Cases 13, 20 and 34) the highest recorded hematocrits were 53, 55, and 54 per cent. The hematocrit of a severely burned female (Case 8) did reach 65 per cent, the highest recorded figure.

Unsuspected hemoconcentration appeared in patients with pulmonary damage and lesser external burns. The hematocrit of two of these (Cases 5 and 19) reached 55 and 59 per cent. This discrepancy was undoubtedly due, in part, to the fact that more attention was paid to prompt plasma administration to those who were severely burned. It is evidence, on the other hand, of the early loss of plasma into the damaged pulmonary bed.

All patients showing a severe degree of the typical burn pattern, burns of the head and hands, developed hemoconcentration and eventually required more plasma in the first 24-hour period than had been calculated by the surface area formula. Massive edema formed beneath the deep burns of the face and scalp in spite of the pressure dressings. The edema fluid was dispersed downward to the neck and over the shoulders and chest. Apparently, in the deeper burns there was a correspondingly deeper damage of the subcutaneous capillary bed with an increasing extravasation of plasma into the loose areolar tissues beneath face, scalp, and downward into the fascial planes of the neck. In the mild burns of the face, such massive edema did not occur and hemoconcentration was not excessive.

* When the hematocrit reading was 60 per cent or over, three units of plasma were given in the four hours before the next hematocrit reading. If the hematocrit was 55 to 59 per cent, two units were injected, if 50 to 54 per cent, one unit.

† Burn shock is defined as low blood pressure shock, with hemoconcentration and diminished blood volume due to loss of plasma fluid into the burn area. Blood pressures below 100 mm. Hg. were recorded on several of the patients in the first 12 hours. One man (Case 26) entered with a blood pressure of 80 mm. He had been sprayed with water and was chilled. His pressure recovered spontaneously within 30 minutes. The woman (Case 2) who had severe anoxia in the first seven hours, in part due to an overdose of morphine, and who received artificial respiration through an intratracheal tube, showed an irregular blood pressure curve with several systolic readings below 90, and one of 70. (She developed auricular fibrillation) The other patients with low blood pressures exhibited them, for the most part, for only short periods. Dr. Aub. seeking to investigate shock, was unable to find a patient with a sufficiently low pressure for a long enough time during the first night to make study worth while. Blood pressures were recorded during this time in all except two patients (Cases 13 and 34).

In spite of the possible inadequacy of the surface area formula when it is applied to burns of the head and scalp, this formula has much to recommend it. It is true that different degrees of burn may result in different amounts of edema but it is still true, roughly, that the amount of plasma fluid lost from the circulation into the tissue spaces is proportional to the area of the burn. The formula is simple to calculate and can be done rapidly, facilitating the handling of many patients. No blood determinations are necessary and it can be applied when laboratory facilities are not available. The complicated formulae of Harkins,¹ and Elkinton, Wolff and Lee² are not satisfactory merely because laboratory determinations and calculations are necessary in order to apply them.

There is a fundamental difficulty to the use of these formulae and also to that of Black. These three formulae tell at the specific moment the blood determination is made how much plasma is required to bring the plasma volume back to normal within a short interval. They do not allow for the amount of plasma that will leak out of the circulation over the ensuing hours. If one of these formulae is applied soon after the burn, when the patient has just entered the hospital, and but little hemoconcentration has occurred, an inadequate amount of plasma will be given. On the other hand, if the formula is applied when the maximum edema has already occurred, an unnecessarily large amount of plasma may be injected, for at that time the rate of plasma loss is diminished. Any formula made on a given blood determination must also take into account the expected loss in the hours to come and this can only be estimated on the basis of the surface area burned. A combination of the two methods is the best.

A difficulty which was partly anticipated but not adequately solved in these patients was the problem of the amount of plasma and intravenous therapy required by a patient with pulmonary damage. After the arrival of the first 15 patients it was obvious that some type of pulmonary pathology was present. At first sight, it was thought that there must have been an explosion and that the pulmonary damage was due to the blast. The intravenous solutions of saline and glucose which were already running into the patients were slowed to a minimum while awaiting delivery of the plasma from the bank. This was done in an effort to prevent the appearance of pulmonary edema in the damaged lungs.* Already several casualties,

* Both sodium chloride and glucose are freely diffusible through the capillary wall in contrast to the plasma proteins which are only partially or slowly diffusible. In the area of a burn or chemical inflammation, the capillary permeability is increased and plasma proteins pass out more freely into the extracellular spaces along with the water and electrolytes to form the edema fluid. Saline or glucose solutions, by raising blood pressures in burned patients, tend to wash more plasma protein out into the area of injury and increase the edema. Since only a portion of the plasma proteins leak out of the capillary, an injection of plasma is more efficient than saline in maintaining blood pressure in burn shock and if given slowly will not cause as rapid a formation of edema.

SHOCK

Obviously suffering from anoxia, had died within minutes after their arrival. As casualties arrived who were able to serve as reliable witnesses, it became clear that there had been no explosion, that only irritating fumes and heat were the cause of the pulmonary inflammation.†

In spite of the early signs of pulmonary damage, plasma was given to most of the patients. Each patient was watched carefully and it was withheld from those who, on the basis either of the mildness of their surface burns or lack of hemoconcentration, apparently did not require it. With the progression of pulmonary signs, however, more caution was exercised. After three patients had died with signs of pulmonary edema the policy of allowing a certain amount of hemoconcentration to persist was resolutely adhered to in all patients with lung damage. The hematocrit readings were maintained around 50 per cent.

Whether the dehydration regimen was of benefit is questionable. It was not sufficiently severe to eliminate kidney function and perhaps was of no detriment. On the other hand, four more patients died with signs similar to those of the earlier three. In three of these latter patients, postmortem examination revealed damage incompatible with life, due to tissue damage in the bronchioles rather than to edema. It is still an unsettled point but if we were faced with the same condition again we would probably allow a little hemoconcentration to persist throughout the period of progressive pulmonary signs.

Normal kidney function was maintained in all but three patients in spite of the hemoconcentration which was allowed to the patients with pulmonary complications. Normal kidney function is assumed when the blood non-protein nitrogen was within normal limits, the urine volume adequate, and the disappearance of hemoglobinuria and albuminuria at the end of two weeks. No renal function tests were performed.

The nonprotein nitrogen of the blood was determined daily from the second through the fifth day in all patients who remained in the hospital, and then every other day or as indicated. Nonprotein nitrogen values above normal were recorded on six patients. In one patient (Case 38) who vomited nearly everything taken by mouth for the first six days, abnormal nonprotein nitrogens of 51 and 62 mg. were recorded on the third and fourth days. In two of the patients who died on the third day (Cases 25 and 27) the nonprotein nitrogen rose just before death to 64 and 78 mg. These are the three

From the same point of view, the physiologic saline solution used in equal volume to dilute the plasma was omitted after the first 36 hours. Fifty per cent glucose was substituted, 50 cc. for each 150 cc. of plasma, in order to maintain the free flow of the plasma. (The flow of undiluted plasma is sluggish.)

† The similarity of the pulmonary signs encountered in this disaster to those of the Cleveland Clinic fire of 1929, was not at first apparent. We had thought of that catastrophe as unique and that with the change in chemical composition of roentgenographic films, similar irritating poisonous nitrogen gases would not again be encountered in civilian life. The clinical course of these patients was also comparable to that seen in soldiers following phosgene inhalation in War I.

patients considered to have had diminished renal function. Two of these three patients had additional signs of abnormal kidney function. Case 38 showed albuminuria and Case 27 both albuminuria and massive hemoglobinuria. In Case 25 the urine findings were normal.

The other three patients in whom an elevated nonprotein nitrogen was recorded were Cases 4, 8, and 36. In Cases 4 and 36 the nonprotein nitrogens were elevated on a single occasion, 62 and 44 mg., respectively, on the fourth day. The hematocrit and serum protein determinations on

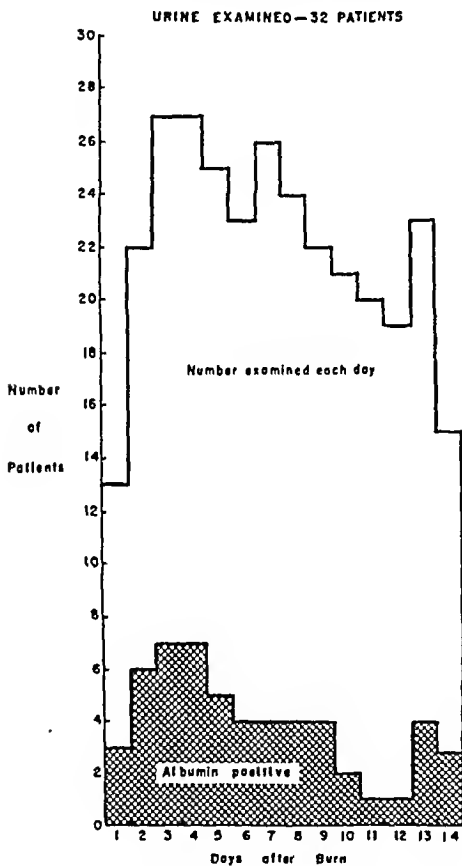


FIG. 43.—The occurrence of albuminuria in 32 patients.

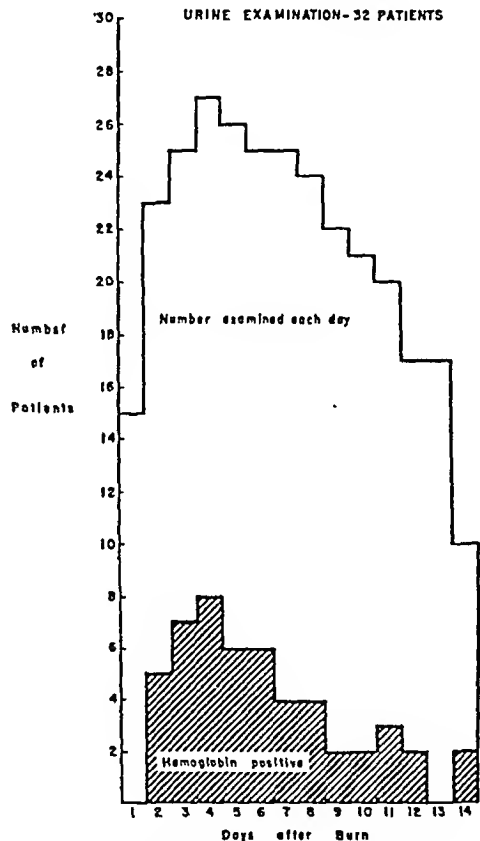


FIG. 44.—The occurrence of hemoglobinuria in 32 patients.

both of these patients were normal on that day. The final abnormal non-protein nitrogen reading was 51 mg. in Case 8 on the seventeenth day; the hematocrit was 35 per cent and the serum protein 7.3 mg. The patient had received a transfusion the day before and received another on each of the next two days because of the low oxygen carrying capacity of the blood. In none of these three patients were there other signs of abnormal kidney function such as albuminuria, hemoglobinuria or diminished urine volume.

Albuminuria occurred in 12 patients, see Figure 43. This includes one of the patients who died. No patient showed albuminuria after the second week. It is noteworthy that the period of albuminuria coincides with the period of resorption of edema of the burns. It cannot be con-

SHOCK

cluded, however, that the protein of the edema fluid is necessarily excreted by the kidney as albumin, for several of the patients with massive edema exhibited no albuminuria.*

There was no absolute correlation between the albuminuria and the type of lesion. It appeared in six of the nine patients surviving with extensive burns and in one who did not. It was found in the girl with pulmonary damage and no external burns (Case 6), and in three patients with minor burns, one of whom was jaundiced. It also occurred in a man with moderate burns and pulmonary damage.

Hemoglobinuria was recorded in nine patients. In one who showed a mild degree it was probably caused by the sulfadiazine, for there were concomitant crystals, and this patient alone of the nine did not show albuminuria. In the other eight, no sulfadiazine crystals appeared during the period of hemoglobinuria. In these eight the time incidence was much the same as that of the albuminuria (Fig. 14). Five of the eight had massive hemoglobinuria; the urine was grossly dark brown to almost black. One who had it (Case 27) died on the third day. The other three showed only slight to mild amounts of hemoglobinuria and it is possible that in these the sulfadiazine may have been the cause except that the hemoglobinuria ceased even though the sulfadiazine was continued. Since but one of the group died and none of the surviving patients has shown any clinical evidence of impairment of renal function, hemoglobinuria *per se* does not necessarily result in renal damage.

It is probable that the hemoglobinuria in the patient who died was a coincidence rather than a contributing cause of death. At postmortem examination of this patient the kidneys were found to be congested with occasional petechial hemorrhages, but there was no evidence of renal damage.

Experimental evidence is accumulating to show that the liver plays an important rôle in the body's compensation to shock. An examination of liver function, therefore, following a shocking procedure, such as a burn, may be of importance in determining the character of a patient's response. Measurement of the prothrombin time was made on all patients on the third and fourth day, and subsequently in a few; in only three patients was the time prolonged. In one man who was severely burned (Case 11), on the fourth day the clotting time was 30 seconds, that of the control 20. These identical findings were recorded on Case 32 on the same day; on the following day she was jaundiced with a van den Bergh of 7.3 mg. The

* The coincidence of albuminuria and resorption of edema is a strong point in favor of the protein of the edema fluid being the source of the albumin. Dr. Zamecnik, at this hospital, has determined increased peptidase activity in human bleb fluid from burn blebs and in lymph flowing from the burns of dogs. Peptidases might alter the proteins of the edema fluid in such a way that they would be excreted by the kidney rather than reutilized. That the greater portion of the extravasated protein is made use of in the organism rather than excreted is proven by the decreasing excretion of nitrogen by the kidney during the period of resorption of edema. (See Nitrogen Balance under Metabolic Observations)

third patient with an abnormal prothrombin was Case 27, who on the third day, the day of death, had a time of 36 seconds, the control 24.

The patient recorded above with the elevated van den Bergh was the sole patient exhibiting jaundice. She had had a severe and prolonged anoxia resulting in damage to the central nervous system. The initial attack of jaundice disappeared completely in a few days but a month later, when she was receiving no sulfadiazine, she had a recurrence of jaundice with a palpable enlargement of the liver. This attack also subsided but not until after two weeks. The origin of this jaundice and hepatitis was undetermined. It can be postulated that it was initiated by prolonged anoxia.

Hemolysis was observed in only one patient (Case 34). She was extensively and deeply burned with large areas of charred skin. She died on the second day. The origin of such hemolysis is not clear. It is possible that it is the result of the actual heating of the blood present in the tissues at the time of the burn.*

Intestinal ulceration and bleeding are common sequelae of burn and other forms of shock. The origin of the lesions which give rise to the bleeding is not clear. It is possible that they are the result of anoxia of the mucosal surfaces due to capillary stasis. The stasis may be due to hemoconcentration with increased viscosity of the blood or to diminished blood flow following arteriolar constriction. Arteriolar constriction and diminished blood flow are known to occur in various parts of the body as compensation for the diminished circulating blood volume and are an effort on the part of the body to diminish the capacity of the vascular bed to make up for the shortage of available blood volume.

In either case the incidence of intestinal ulceration and hemorrhage might be considered an index of successful shock therapy. Figure 45 shows the number of stools with a positive guaiac test. None of the stools was grossly bloody or tarry. It is interesting that Case 38, with the prolonged vomiting, did not show blood. Those which were positive for blood were found in patients with all of the different types of lesions. The largest amount of blood recorded was in Case 20, who showed a +++ test on the seventh day. At this time the hematocrit was below normal and whole blood transfusions were subsequently required. She had extensive deep surface burns and it was not believed that the loss of blood in the intestinal tract significantly contributed to the progressive anemia.

An unexpected finding of interest was the occurrence of alkalosis in two patients. On both the third and fifth days, an arterial puncture was done on Case 6, the young girl with pulmonary lesion and no surface burns. The p_H 's were 7.63 and 7.40, and on the first blood the CO_2 was 30.3 m.eq.,

* In the experimental laboratory we have learned to associate hemolysis with the severity of the burn.³ Hemolysis is not encountered in dogs with hot water burns of the extremities when the temperature of the water is less than 100° C., or when at 100° C. it is applied for 15 seconds or less. At 100° C. it appears if the burn is for 20 seconds, and invariably if the burn is 30 seconds or longer.

SHOCK

and the oxygen content 17 vols. per cent. On the second blood, the sodium was depressed at 138.6 m.eq., whereas the other findings were normal: Total base 152.5 m.eq., calcium 9.0 mg., chloride 100 m.eq., phosphate 4.3 mg., phosphate 4.3 mg., and hemoglobin 12.7 Gm.

A second patient (Case 13) with both extensive severe skin burns and moderately severe pulmonary complications, showed an alkalosis as well as an anemia on the fifth day. An arterial puncture was made to determine the oxygen content because of the falling hematocrit and progressive anemia.

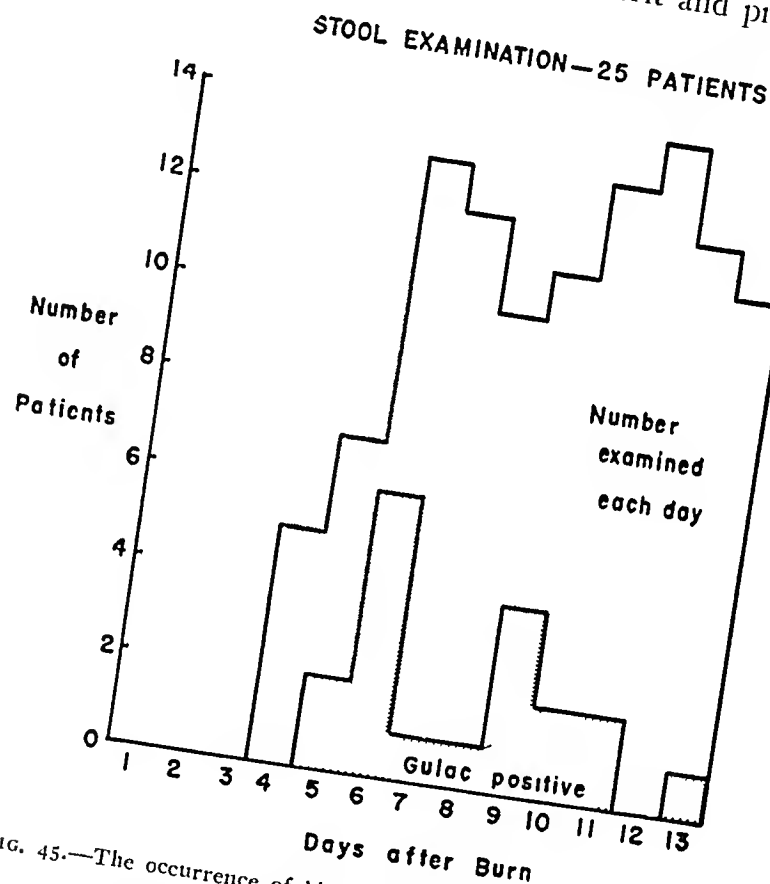


FIG. 45.—The occurrence of blood in the stools of 25 patients.

The hematocrit was 38 per cent, hemoglobin 9.4 Gm., and pH 7.47, non-protein nitrogen 24 mg., the total base 147 m.eq., sodium 133 m.eq., calcium 9.3 mg., chloride 97 m.eq., CO_2 content 28.5 m.eq., phosphate 1.7 mg. The phosphate was low presumably because the patient had eaten recently. The oxygen capacity was 14.6 vol. per cent, content 13.1 vol. per cent, or a saturation of 89.8 per cent.

The alkalosis in these patients was due presumably to the sulfadiazine therapy,⁴ and not to the pulmonary complication. For the probable origin of the progressive anemia, see below under *Maintenance of Nutrition*.

Chemotherapy.—Chemotherapy to effect bacteriostasis is an integral part of the modern treatment of burns. At the moment, the sulfonamide preparations prevail; unfortunately, they occasionally lead to untoward results and disturb organ function and metabolism. Since the maintenance of normal bodily function is part of good shock therapy, any discussion of the treat-

ment of shock in burns must needs include chemotherapy. It has been pointed out above that sulfonamide therapy leads to a loss of base and to alkalosis but this is apparently of little import. It is the kidney and liver damage which occasionally occur even without overdosage which are of greatest significance.

The relation of infection to shock in burn patients has been but little explored scientifically. Our present clinical impression is that infection is often culpable. It is possible that the shock, even as soon as in the late hours of the first day, is in part due to the toxemia of bacterial infection. Certainly in later days infection supersedes in responsibility all other factors. The malnutrition and anemia (see under *Maintenance of Nutrition*) are almost certainly of infectious origin.

There is also a reciprocity between shock and infection. In shock, due to a disproportion between the available circulating blood volume and capacity of the circulation resulting in decreased blood flow to tissues, anoxia inevitably develops. It is well known that certain organisms, including the *beta* hemolytic streptococci, multiply faster in even slight degrees of anoxia. In burn wounds, therefore, in which any degree of anoxia exists, organisms multiply more rapidly and infectious toxemia develops relatively early.

Such thoughts only emphasize the importance of minimizing bacterial contamination of the burn wounds by immediate coverage of the surface.*

Maintenance of Nutrition.—In the treatment of burn shock every effort should be made to administer the necessary fluid and protein through the gastro-intestinal tract. Patients with less than ten per cent of the body surface burned, particularly if mildly, and if they are not nauseated or vomiting, may be treated by this route. They should drink readily digestible fluids with a high protein content. Milk and milk products, high protein bouillons with amino-acids added are such fluids. Warning should again be made that if there are deep burns of the face and scalp, particularly if there are acute pulmonary lesions as well, there may be an unexpectedly great loss of plasma volume and intravenous plasma therapy may be required. Ten of the patients, some with mild burns, and some with pulmonary damage only, were treated entirely by mouth.

High protein therapy by mouth is not sufficient. A caloric intake sufficient for maintenance is advisable. It is probable that a moderate carbohydrate intake is required for normal liver function.

Attention to the necessary accessory food substances is also imperative. All of the patients received large doses of the vitamins, both as natural and synthetic substances, from the first day. In some, these substances had to be given intravenously. It is to be remembered that patients with severe burns, even with minimal infection, have fevers, that their metabolic rates

* The availability of sulfonamides to the burn wound has been considered in a previous paper on the surface treatment. Sulfonamide levels in bleb fluid were recorded on five patients (Cases 17, 19, 20, 28, and 38). Levels, together with the simultaneous blood levels, are available in the protocols.

SHOCK

are, therefore, elevated, and their requirements both for total calories and accessory substances are increased. For the patients with more active infection this is the more true.

None of the patients developed clinical signs of a vitamin deficiency. They were not weighed on entry but of the 11 patients with severe burns who survived, almost all lost some weight, and two lost a very considerable amount (Cases 11 and 13).

Constant attention was paid to the development of the initial signs of anemia. None of the patients with second degree burns developed clinically significant anemia and none received, therefore, a whole blood transfusion except the woman in whom anoxic damage to the central nervous system occurred. Eight of the ten patients with third degree burns, who stayed at this hospital until healed, received transfusions for anemia. In three, one transfusion sufficed. Another three patients received three, four and five transfusions each. The most severely burned patient to survive (Case 13) received, in all, 25 whole blood transfusions of 500 cc. With this latter patient we faced difficulties:

Her burns were so extensive and the change of dressings so painful that endless time was consumed in clearing the areas of dead tissue. From the fifteenth to forty-fifth days efforts were made to change all of the dressings at one time, and general anesthesia was required each time the dressing was done. The patient was nauseated for each following 24 hours. The nutritional status of the patient suffered and her courage failed. Intravenous amino-acid injections as well as whole blood transfusions were given by femoral vein. (A single vein in one arm was the only other available vein in an extremity). It was not until the dressings were assigned to a single team to be done without general anesthesia for lesser areas at one time, that the patient's nutritional status improved. With the advance in general health, epithelial proliferation across granulating areas became obvious and grafting was possible.

This patient presented psychotic tendencies, and it was not until a rapport was reached between the patient and Dr. Cannon and his two intern assistants that mastery of the nutritional state was achieved. The rapport was abetted by the withdrawal of other physicians who previously had had jurisdiction over aspects of her care. The importance of the psychologic factor in the production of good digestion cannot be too strongly emphasized. All too frequently, where there are many doctors, each responsible for a different aspect of the patient's regimen, the patient is unable to find one physician to whom she can turn.

Adrenal Cortical Extract.—Extract of the adrenal cortex containing the active principle of the gland has been recommended in the treatment of burn shock.^{5,6} The predominant signs and symptoms of adrenal cortical insufficiency both in man and animal are those of shock. Among other findings there are a low blood pressure, hemoconcentration, and an elevation of potassium and phosphate in the blood. Such findings are also characteristic of shock appearing after trauma, burns, intestinal obstruction and sometimes severe infection.

The problem of the relation of the adrenal cortex to burn shock has been under investigation in the Surgical Research Laboratory during the past year.

It has been found that in adrenal insufficiency in the dog there is a generalized increase in capillary permeability. This increased permeability is reversible by the administration of adrenal cortical extract.⁷ In the dog there is also an increase in capillary permeability in the experimental burned area as has been demonstrated by Field, Drinker and White,⁸ (1931), and more recently by Glenn, Peterson and Drinker⁹ (1942). In our laboratory this increase in permeability has been shown to be localized to the region of the burn.¹⁰ Only rarely does an increase in the nonburned area develop following prolonged shock. Efforts to decrease this abnormal permeability by large doses of adrenal cortical extract have failed. Although under different experimental conditions it might be possible to influence the abnormal permeability induced by a mild burn, certainly the adrenal cortical hormone, judged by these experimental results, would appear to have little practical usefulness in burn patients.

From time to time, in this hospital, selected patients with burns have been treated with adrenal cortical hormone in the effort to evaluate this substance. No unequivocal benefit has been obtained from its use. Two of the patients of the Cocoanut Grove were selected for adrenal cortical therapy (Cases 34 and 27). Both of these patients had extensive surface burns and pulmonary injury.

On the afternoon of the first day, when it was clear that Case 34 had severe pulmonary damage, adrenal cortical extract (Upjohn) was started; 50 cc. were given intravenously over a one-hour period. The patient's blood findings before and after receiving the extract are given in Figure 46. She had already received eight units of plasma, and only a minor amount of hemoconcentration had occurred. She was selected for extract therapy in the hope of decreasing pulmonary edema by reducing the capillary permeability in the pulmonary bed.

The patient died six hours after receiving the extract. The course had been progressively downhill, with increasing anoxia in spite of oxygen administration. There was no clinical evidence that the patient had benefited from the extract. Admittedly, the patient's disease was profound and this was a rigorous test for any mode of therapy.

The second patient (Case 27) was also started on extract therapy on the first day, 14 hours after the fire. The blood determinations, before and after

CASE 34

Date	Time	Hemat. %	Pl. Prot. Gm. %	Na m.Eq/l	Cl m.Eq/l	Therapy
11/29/42	2: A.M.	51				
	5:	50	6.8	139	103	Plasma 3 units
	10:	52	7.6			Plasma 3 units
	4: P.M.	51	7.0			Plasma 2 units
	5:25					ACE started
	6:25					ACE 50 cc. finished
	10:	54	7.0	102		
11/30/42	12:50 A.M.		DIED			

FIG. 46.—Adrenal Cortical Extract (ACE): Schedule of administration together with plasma injected and blood findings in Case 34.

SHOCK

extract, are given in Figure 47. Before and during the extract therapy the patient received eight units of plasma. Over a period of 14 hours, 70 cc. of extract were given. She died 35 hours after the last injection of extract. During that period she received an additional five units of plasma. The nonprotein nitrogen which was 28 mg. at the time of administration of the extract rose to 90 mg. before death.

This was another severe test for adrenal cortical extract. The patient had extensive deep surface burns and pulmonary damage; anoxia persisted despite of an oxygen tent. This patient, too, was chosen to treat with extract because of the pulmonary lesion, in the hope that the extract would diminish capillary permeability in the lung bed and thereby reduce the edema. There was no evidence either during or subsequent to the administration of the extract that the edema was less or the aeration of the blood better. The difficulty of clinically evaluating such a substance as adrenal cortical hormone in the therapy of burns or other forms of shock is apparent from the experience with these two patients to whom the extract was administered. Had the two patients survived without the administration of adrenal cortical extract. Had the two patients to whom the extract was administered survived, it would have been as wrong to ascribe their survival to the adrenal hormone as it would be to incriminate the hormone as the cause of their death. There is no clinical evidence that the hormone in any way influenced the course of the disease.

Date	Time	Hemat. %	Pl. Prot. Gm. %	N.P.N. mg. %	Cl m.Eq/l	K m.Eq/l	Diazine mg. %	Therapy
CASE 27								
11/29/42	2: A.M.							Plasma 1 unit
	10:							Plasma 1 unit
	12:40 P.M.	56						ACE started
	2:45	56	8.1					Plasma 2 units
	3:30							ACE 50 cc. finished
	4:							Plasma 2 units
11/30/42	10:	47						Plasma 2 units
	2:15 A.M.	45	6.4					ACE started
	2:45		6.2					ACE 20 cc. finished
	6:							Plasma 2 units
	2: P.M.	43			5.1			Plasma 2 units
	8:45	44	5.8					Plasma 2 units
12/1/42	7: A.M.	42	5.9					Plasma 2 units
	12:15 P.M.	35	5.3	28	102.7			ACE started
	1:55		5.6					ACE 20 cc. finished
				78	113.9			
						8.2		
						7.0		
								Plasma 2 units
								Plasma 2 units
								Plasma 1 unit

FIG. 47.—Adrenal Cortical Extract (ACE): Schedule of administration together with plasma injected and blood findings in Case 27.

CONCLUSIONS

The pulmonary lesion in the casualty as unexpected, and complicated by a cur in civilian

FIG. 47.—Adrenal Cortical Extract (ACE): Schedule of administration together with plasma injected and blood findings in Case 27.

CONCLUSIONS

The pulmonary lesion in the casualties of the Cocoanut Grove disaster was unexpected, and complicated the care of shock. Since such lesions may occur in civilian as well as military disasters, it is well to be prepared to meet them. The treatment of burn shock, usually a straightforward problem of maintaining an adequate plasma volume, had to be modified in an

effort to prevent excessive pulmonary edema. Anoxia, not ordinary surgical shock was the primary concern.

It was fortunate that a treatment of the burn surface had been chosen in advance which permitted a maximum of attention by the personnel available to the problem of shock. Plasma therapy was prompt and effective. There were no deaths in the first 12 hours. The seven deaths that occurred took place within 13 to 62 hours and were the result of the pulmonary complication.

An effort was made to diminish the edema in the damaged lungs by allowing a mild amount of hemoconcentration to persist.

Massive edema, out of proportion to the surface area involved, may occur beneath deep burns of the face and scalp. The use of the various formulae in computing plasma dosage is discussed.

Hemoglobinuria occurred in eight patients; one died with no anatomic evidence of renal damage. The other seven have survived with normal kidney function.

Adrenal cortical extract did not affect the pulmonary edema or the general bodily function of the two severely injured patients to whom it was administered.

REFERENCES

- ¹ Harkins, H. N., Lam, C. R., and Romence, H.: Plasma Therapy in Severe Burns. *Surg., Gynec. & Obst.*, **75**, 410, 1942.
- ² Elkinton, J. R., Wolff, W. A., and Lee, W. E.: Plasma Transfusion in the Treatment of the Fluid Shift in Severe Burns. *ANNALS OF SURGERY*, **112**, 150, 1940.
- ³ Cope, O., Mixter, G., Jr., and Graham, J. B.: To be published.
- ⁴ Beckman, W. W., Rossemcisl, E. C., Pettengill, R. B., and Bauer, W.: A Study of the Effects of Sulfanilamide on Acid-Base Metabolism. *J. Clin. Invest.*, **19**, 635, 1940.
- ⁵ Rhoads, J. E., Wolff, W. A., and Lee, W. E.: The Use of Adrenal Cortical Extract in the Treatment of Traumatic Shock of Burns. *ANNALS OF SURGERY*, **113**, 955, 1941.
- ⁶ Scudder, J., and Elliott, R. H. E., Jr.: Controlled Fluid Therapy in Burns. *South. Med. & Surg.*, **104**, 651, 1942.
- ⁷ Cope, O., Moore, F. D., Mixter, G., Jr., and Graham, J. B.: To be published.
- ⁸ Field, M. E., Drinker, C. K., and White, J. C.: Lymph Pressures in Sterile Inflammation. *J. Exper. Med.*, **56**, 363, 1932.
- ⁹ Glenn W. W. L., Peterson, D. K., and Drinker, C. K.: The Flow of Lymph from Burned Tissue: With Particular Reference to the Effects of Fibrin Formation upon Lymph Drainage and Composition. *Surgery*, **12**, 685, 1942.
- ¹⁰ Cope, O., Moore, F. D., and Tobin, L. H.: To be published.

A NOTE ON THE BLOOD BANK

LAMAR SOUTTER, M.D.

FROM THE SURGICAL SERVICES AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

A BLOOD BANK is a requisite for the efficient handling of patients in a disaster. In the first place it is economical. In the second place, with burn casualties particularly, it is imperative to feel free to administer all the plasma necessary. There need be no restraint in the use of frozen plasma. Dried

THE BLOOD BANK

plasma, with its content of mercurial preservative, offers a drawback, since, theoretically, kidney damage may result if too much is given.

Supplies on Hand.—At the time of the Coconut Grove fire the Massachusetts General Hospital had 391 units of sterile frozen plasma in its own bank, 38 flasks of whole blood, 106 units of dried plasma, and a reserve of 76 units of frozen plasma stored for emergency use at the Faulkner Hospital seven miles away. This meant a total of 611 potential transfusions. The frozen units stored in 500 cc. Fenwal containers were diluted half and half with normal saline.

For thawing we had three large tin pans in which the bottles could stand while a current of water at body temperature surged around them from a faucet. The temperature was controlled by hand with a water bath thermometer.

In our central supply room were kept stored in dust-proof containers 48 sterile packages consisting of intravenous tubing all connected to Fenwal vent tubes, Baxter filters, and glass adaptors. In the same package were the usual shut-off clamps, two No. 19 and No. 18 needles in a test tube, and an adaptor for making a connection with a needle to a Strumia bottle. In our emergency supply room were a large number of poles to support infusion bottles, as well as gauze, splints and bandages.

System of Administration.—The administration of fluids began with a saline infusion started through an intravenous apparatus and later through the plasma sets with Baxter filters. As soon as plasma was available, 60 minutes after the arrival of the first victim, these saline flasks were changed to plasma. In many instances the plasma transfusions were started before the patients left the emergency ward to go upstairs to the floor cleared for their use. A selected group of three interns was assigned to start transfusions and keep them going. They went from bed to bed setting up apparatus or assisting the team in charge of the patient if it was having difficulty.

Veins Used.—The system of fluid administration at the hospital has in recent years been one of using the most peripheral veins first, usually those on the back of the hands. A sharp No. 19 or No. 20 needle is inserted for administration of saline and glucose, but at least a No. 19 for transfusions. Cannulae, involving frequent subsequent destruction of veins are rarely used. The extremity is carefully splinted and the needle well strapped to it. The needle is inserted with the aid of a glass adaptor rather than a syringe.

On the night of the fire this policy was employed, but because of the number of arm and hand burns, a very high percentage of foot and leg veins were used. These are in an area difficult to splint. They are often at an angle which impedes the insertion of the needle and subsequent fixation. Furthermore, the situation was made worse by the patient being transported from the emergency ward, by their restlessness, and their being turned for the application of dressings. It was necessary to cut down on the veins of eight patients during the first night and insert cannulae. They were only of temporary help, particularly in instances where the plasma had already

run in; a decision had to be made whether more plasma was to be given, or saline or dextrose solution to keep the needle open. This also pertained to people with difficult veins who had a needle well inserted. It meant that some people received more saline than was wise.

System of Filtering.—The filters occasioned us little or no trouble. Although we have found that whole blood undiluted by saline will stop in over five per cent of transfusions through Baxter filters, the dilute plasma used for these victims flowed well. In several instances, when the complaints of malfunctioning of the apparatus were laid at the door of the filter and it was changed and inspected, the amount of clot within it filled less than one-half of the filter, and a change of the filter drip brought no improvement. In one case a patient received eight units through the same filter without stoppage.

Slow flowing after an initial rapid drip was noted in many instances. This was usually in leg veins which were small and tortuous. We blamed this slow flowing, when dextrose ran well, upon the relative gummy nature of the plasma. In other patients constricting pressure bandages or theoretically elevated venous pressure due to extensive pulmonary burns were blamed for this phenomenon. We inserted a three-way stop-cock in the line between filter and needle for Case 27, enabling us to use a syringe as a pump for more rapid infusion. This was successful, though it may tend to increase clot formation, and for whole blood would be dangerous because of cell fragility. We tried this in other instances and have now adopted it as routine for our plasma sets.

Handling of the Supply.—The supply of thawed plasma was controlled by telephone communication with the bank. As the original 16 units were melted, more plasma was started and was sent to the wards as rapidly as possible. We tried to keep about ten flasks on hand at all times in the first six hours. After that the administration was not on an emergency basis, so that we only thawed what was needed. A total of 147 plasma transfusions was given, 120 in the first 24 hours, 19 in the second, and eight in the third.

The work in the blood bank was started by an able medical student on call for night groupings and cross-matchings. He was soon assisted by a blood bank nurse, two other nurses, and several interns. The melting pans are important. We now have two smaller ones, divided into 16 sections to keep the bottles from tipping, with an overflow to run into a sink. The records of the pools used were well kept in the bank, but, unfortunately, time was too pressing on the wards to note the number of each bottle administered to each patient.

Remaking the Plasma.—There was an immediate appeal made for donors. This was greatly aided not only by radio announcements, but by the zealous action of two conscientious objectors, residents in the hospital for metabolic studies, who went out into a neighboring street, stopped passing traffic and asked for all to come in and give their blood. We had over 100 donors, many of whom had unfortunately been eating or drinking too recently, but

THE BLOOD BANK

we had sterile sets enough to take 23 bloods. For the next week we received nothing but voluntary donors so as to remake our plasma. Because of a wonderful response and the help of the Red Cross, which in the following week received more blood than they could ship, and hence supplied many hospitals with it, by the end of two weeks of very hard work we had made a total of nearly 300 flasks for our reserve for civilian defense. Ordinarily we make but 65 units a month. Our fears that use of plasma in a disaster would leave us depleted were unjustified.

Follow-up Thoughts.—Our follow-up on the work done gave the following results: First, there were no reactions. That is, there were no chills reported, but possible temperature changes were masked by the pyrexia following the burns. There was but one patient with jaundice though others received plasma from the same pool without untoward effect. Second, we felt that too much saline was given, although the maximum administration to any patient was 2,250 cc. in 24 hours. It was possible that much more might have been given and that this amount of sodium chloride was inadvisable. We began to dilute our plasma with 50 cc. of 50% dextrose in the first pools made immediately following the disaster. Using fresh centrifuged blood, these pools were being used within 38 hours after the fire. Third, our 48 plasma sets complete with filters were too few for adequate service in obtaining resterilization, we would have run short. Now the number has been doubled and stop-cocks inserted between filter and needle. Fourth, the amount of fibrin clot was very small and was a nuisance in only two cases. Fifth, we had some vein complications. The early ones were local infection as a result of improper care of the wounds in two cases and a slough for the same reason in the one sternal administration of plasma. The vein thromboses are discussed elsewhere.

A NOTE ON THE THROMBOPHLEBITIS ENCOUNTERED

FRANCIS D. MOORE, M.D.

FROM THE SURGICAL SERVICES AT THE MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASSACHUSETTS

VIRTUALLY all of the factors which predispose to the formation of thrombi in the veins of the leg, are present in a patient recovering from a burn. Shock with decreased blood flow and lowered venous pressure, hemoconcentration with increased blood viscosity, prolonged immobilization, circular dressings, injections into the veins of the leg, sepsis, edema, and nutritional deficiency may all be expected to contribute to some degree. Of the 39 patients cared for, in this hospital, following the Cocoanut Grove disaster, five presented thrombo-embolic phenomena of clinical significance. This represents an incidence of 13 per cent. However, of the nine patients hospitalized for a prolonged period and requiring grafts to third degree burns,

four developed evidence of thrombosis of the leg veins, an incidence of about 45 per cent. Two of these presented roentgenologic evidences of a pulmonary infarct.

A word of explanation is necessary in regard to both the terminology used and the policy of treatment. The term "thrombophlebitis" is used to indicate an acute inflammatory process in the veins of the leg attended by local pain, tenderness, warmth and some systemic reaction. The term "phlebothrombosis" is used to cover those cases in which a bland clot is present in the veins, with minimal inflammation and adherence. In both groups the presence or absence of swelling depends on the level and extent of the involvement; gastrocnemius spasm ("Homan's sign") may or may not be present depending probably on the degree of perivascular reaction.

It has been the policy at this hospital for several years to treat both of these conditions by ligation and division of the involved veins, usually the superficial or common femoral vein. This ligation is carried out below the profunda femoris junction providing the common femoral is not involved. Where the thrombophlebitis involves the superficial saphenous system, ligation of the great saphenous at the saphenofemoral junction is considered adequate unless there is evidence of involvement of the deep system. Diagnostic roentgenograms, using the intravenous injection of diodrast ("venograms"), have not been made because experience has shown that these are often misleading and the procedure is irritating to the intima of the veins. Anticoagulants, such as heparin or dicoumarin, have not been used because it is felt that these do not affect either the established thrombus or infarct, that they only prevent further extension of thrombosis, and that, therefore, they do not guard against fatal embolism.

The patients of this series who showed thrombo-embolic phenomena are of considerable interest because they represent the whole spectrum of this group of diseases, ranging from the patient with pulmonary infarct and no local signs in the legs, to the patient with fulminating local thrombophlebitis but no pulmonary manifestations. Furthermore, they show the *modus operandi* of some of the predisposing factors in this group of conditions, factors which may be eliminated by more meticulous attention to details of the patients' regimen. There follows a brief narrative of the development of the venous complications in these five cases.

CASE REPORTS

Case 2.—This was a slightly built woman, with poor muscular tone, who moved about in bed seldom during her convalescence unless urged to do so. The dressings on her right leg, where there were small second and third degree burns at the knee and ankle, were covered during most of her convalescence by a continuous spiral elastic bandage from toes to groin. However, her left leg was burned at the knee and despite precautions to the contrary she was found to have been dressed with a circular bandage with no lower-leg component, on several occasions. At the time of entry, due to the presence of burns on both arms plus the fact that she was in an oxygen tent for some time, she had an intravenous infusion placed in her saphenous vein in the left ankle. Operative procedures to graft her left hand were carried out on December 26, January 9, and January 15. These included a skin graft which was taken from the left thigh; this donor site was dressed on one occasion with a tight circular bandage, later replaced with a bandage extending to the foot. At no time during this period were the patient's feet elevated, or was she on regular bicycle exercises.

THROMBOPHLEBITIS

On January 14, the Roentgenologic Department suggested that her previous pulmonary picture now showed a superimposed process most likely due to a small infarct, and on January 18 this was confirmed by the finding of a friction rub at the right base. Examination of the legs at this time was completely negative except for the superficial burns and wounds previously mentioned. However, with established infarction in her right lung and no other demonstrable source for the emboli, it was felt that she had a phlebothrombosis in the calf veins of her legs and that ligation should be carried out. Therefore, on January 19, a bilateral ligation of the femoral veins below the level of the profunda, was performed. At this level no clot was found and free bleeding was encountered from both directions. Following this operation no further infarcts were found clinically or roentgenologically, and within a week her chart became flat and remained so until discharge four weeks later. When seen two months later her ligation wounds were well healed and she had no swelling or discomfort of any kind in her legs.

The phlebothrombosis presumably present in this patient resulted from many factors, among which her prolonged immobilization and circular thigh bandage were outstanding. Although she was in shock for a period after entry, and had received an injection in her saphenous vein, the long (eight weeks) interval between these events and her infarcts suggests that they were not causes of the thrombotic process. Bicycle exercises or elevation of the foot of her bed, as well as better bandaging, might have helped ward off this complication. Once discovered, the therapy seemed to be effective in preventing recurrence, and her chest quickly cleared.

Case 36.—A man of 28, who was an active newspaper reporter and feature-writer prior to the fire, was a vigorous and muscular male who in his early stay in bed was very active and moved about considerably. Burns on his hands were grafted on December 22 and January 2, and because of a desire to get him mobilized as soon as possible he was allowed to get out of bed and start walking again on January 7, five weeks after the fire. Despite repeated admonitions not to do so, he persisted in sitting in a chair instead of walking about. This position, without footstool or leg elevation of any sort, resulted in dependency of his legs and possible pressure in the popliteal space. The dressings of his thigh donor sites on the left side were properly applied and carried down to the toes. One week after he had been allowed out of bed he complained of pain in his left leg. Examination showed tenderness in the calf, and during the three hours after onset the size of this calf increased five-eighths of an inch. On the following morning these signs persisted and he had developed, in addition, an interesting variant of the Homan's sign. Not only was the calf painful and limited in dorsiflexion, but also his gastrocnemius muscle was in such severe spasm that he had fully developed ankle clonus. The temperature of this leg was increased and his white blood cell count was 18,000. His temperature was normal. His lungs were negative on clinical examination. A diagnosis of left thrombophlebitis was made and, on January 14, a left superficial femoral vein ligation was carried out, below the level of the profunda. The vein is opened routinely in this procedure and in this instance a large clot was removed by aspiration and free bleeding obtained. The clot had progressed upwards to within 1 cm. of the junction with the profunda femoris. There was considerable perivascular edema and thickening. His postoperative course was satisfactory, and he was discharged 11 days later. At two months he had untoward leg symptoms.

The diagnosis of left-sided thrombophlebitis in this case was fully substantiated by the operative findings. The clot found was nonadherent at the level exposed, though presumably it was adherent lower down. According to our usual procedure the other leg should have had the same operation, but the signs were so clearly unilateral, that it was felt justifiable to limit the operation to the one side. Of the various predisposing factors in this case, the relation to his mobilization and habit of sitting in his chair, leaning forward and listening to the radio, stands out as most significant. The thigh bandage over the donor site and the long period in bed no doubt also played a part. He was never in shock nor did he have any intravenous infusions in his legs. His lack of pulmonary infarcts is probably traceable to the inflammatory nature of the process, with resultant adherence. The fact that the clot was free at the level of ligation, however, suggests that operation may well have prevented a subsequent massive embolus.

Case 11.—A 24-year-old male, sustained extensive burns of his back. Because of pain he lay quietly most of the time. To facilitate moving about he was given a foot-board to press against, and a Balkan frame with hanging handles to lift himself, using his one good hand. On December 25, four weeks after the fire, he complained of chest pain and raised a little bloody sputum. However, his chest films were repeatedly negative and it was thought that his tracheal burn was giving rise to the blood-streaking. His legs were normal to examination save for the burn on the right knee. On January 5, grafts were taken from the left thigh and put on his arm and right knee. A snug circular bandage with no lower leg extension was applied to the knee graft. The next day this was discovered and rectified but in the interim the patient had had 18 hours of partial venous obstruction to his right leg. Within three days he developed soreness and swelling in the right calf. An exploration of his right femoral vein was made on January 8.

Because of the presence of unilateral signs and a unilateral causative mechanism (the tight dressing) it was considered permissible to depart from established precedent as in the previous case, and operate on only the one side. At operation the vein was found to be thickened and edematous, but with no clot at this level. Slow bleeding from below suggested a clot further down but none could be obtained with the Trendelenburg sucker.

He remained quite immobile in bed despite efforts to the contrary. On February 3 (nine weeks after the burn), he complained of pain in his left groin and rapidly developed a fever, palpable tender lymph nodes and a tender cord along the course of one of the thigh tributaries to the deep system. Despite these signs of an acute inflammatory process in the thigh he had no ankle edema or Homan's sign. The diagnosis of left-sided femoral thrombophlebitis was made and a left femoral exploration carried out.

At this operation an unusual situation was found. His left femoral vein was almost an inch in diameter, surrounded by considerable edema, with a wall 3 mm. thick. Many large nodes, up to 2 cm. in diameter, were in the femoral triangle. Large clots were aspirated from the superficial femoral and profunda branches. The common femoral vein was ligated above the entrance of the profunda. The saphenous was also tied because of involvement at its orifice, but tied proximal to the entrance of the superficial epigastric vein so that a continuous superficial channel was left, running up to the epigastric system. Postoperatively, the patient did well; and when seen two months later he had no swelling or leg symptoms despite the extensive ligations on the left. He never developed any roentgenologic evidence of pulmonary emboli.

THROMBOPHLEBITIS

This patient evidently had phlebothrombosis of his right leg and later developed an acute thrombophlebitis in the left thigh. The right leg pathology was unquestionably furthered if not caused by the tightly applied dressing at the knee. The cause of the acute process on the left is hard to assign to any one factor, but was undoubtedly a result chiefly of prolonged immobilization. The donor sites on the left leg were well healed at the time of onset of the acute thrombophlebitis.

Case 8.—A 29-year-old housewife, was slightly built and of little natural muscular vigor. Left to her own resources she lay quietly in bed making no effort to move about. During her first 18 hours in the hospital she had had a cannula tied into her left long saphenous vein. She often had the head of her bed and the knee-rest raised with her legs slightly flexed. This produced pressure in the popliteal space and the flexion at the hips presumably increased the venous pressure in her left shoulder, but her chest was weeks after the fire, she complained of pain in her left shoulder, but her chest was banded and clinical examination was unsatisfactory. Therefore, a roentgenogram was taken, which was interpreted as consistent with an infarct at the left base, with possibly a second one behind the heart. Examination of her legs at this time was completely negative. Because of the fact that no other source for the emboli could be demonstrated it was felt that the presumptive source was the great veins of the leg. Therefore, bilateral femoral vein ligation was decided upon.

This was carried out the same day, and on opening the veins, no clots were found. Postoperatively she did well, and developed no more infarcts. Two days after the roentgenogram mentioned above, another one was taken which showed that she had developed a small amount of fluid at the left base, making even more likely the previous diagnosis of infarct.

This patient falls into the group in which pulmonary embolism pointed to a thrombotic process in the legs, and the absence of local signs made a diagnosis of phlebothrombosis presumptive. Immobilization and position in bed probably contributed as much to her troubles as any other factor. Although she had had a cannula tied into a saphenous vein, an interval of four weeks had passed between this and the emboli, and she never showed any saphenous pathology clinically. She had no burns on her legs and prior to her embolism had no grafts taken from the thighs.

Case 14.—This patient developed a typical acute saphenous thrombophlebitis in his left leg eight days after the fire. He was lightly burned and had not been systemically ill since 48 hours after the fire, and had been up and about the ward. However, he had had an intravenous needle placed in his long saphenous vein at the ankle in his first few hours in the hospital. Through this vein had been infused about 1,000 cc. of 5 per cent glucose in saline, and 1,000 cc. of plasma. On December 7, he noticed a sore red streak up the leg from the intravenous site at the ankle. There was a palpable tender cord along the course of the saphenous vein. Therefore, the saphenous vein was tied off at the saphenofemoral junction, to guard against extension of this process up into the femoral and iliac system. The patient did well postoperatively; his local process quieted down on rest and heat; and three days later he was discharged to an Army hospital.

This patient is of interest in that he was the only one of many who received injections into ankle veins, who developed saphenous phlebitis.

DISCUSSION

From time to time it became necessary to perform femoral vein punctures, either to get blood for study, or to give intravenous infusions in patients in whom other veins were not available. This was done in seven patients (Cases 13, 40, 32, 27, 34, 23, and 8); in only one did thrombosis develop (Case 8), and there was such a long interval between the femoral vein puncture and the development of the thrombosis, that it is probable that there was no connection between the two. One of the patients (Case 13) is of especial interest because she had at least eight femoral vein punctures as well as extensive septic burns on both legs. She never developed any evidence of pulmonary infarction. Examination of the calf veins was impossible due to the overlying burns.

The presence of burns or sepsis in the legs does not seem to predispose to thrombosis providing, of course, that the sepsis does not progress to the point of involvement of the larger blood vessels. However, lesions on the legs may be an indirect cause of venous complications if tight circular bandages are used which obstruct and distend the venous system distal to them. Of the five patients in this group with thromboses, only two had leg burns.

CONCLUSIONS

It is felt that patients who have been severely burned are prone, in a rather high percentage of cases, to develop thrombo-embolic phenomena from the veins of the legs. Constant vigilance must be exercised particularly in relation to prevention. The position of the patient in bed, and mobilization in bed with measures taken to ensure adequate venous circulation, are important factors in preventing thrombosis and embolism. When leg signs are positive, or evidence of pulmonary infarction is present, the treatment of choice is immediate ligation of the involved veins.

METABOLIC OBSERVATIONS*

✱. OLIVER COPE, M.D., IRA T. NATHANSON, M.D.,
G. MARGARET ROURKE, A.B., AND HILDEGARD WILSON, Ph.D.

FROM THE SURGICAL RESEARCH AND JOHN COLLINS WARREN LABORATORIES, HARVARD UNIVERSITY, AT THE
MASSACHUSETTS GENERAL HOSPITAL, BOSTON, MASS.

A STUDY of the nitrogen metabolism and its relation to the adrenal cortex and 17-ketosteroids in burn shock was already under way in these laboratories prior to the Cocoanut Grove disaster, in the hope of elucidating some of the problems under discussion in recent years regarding the body's compensation to injury. Selye,¹ working with experimental animals, has called such compensation the "alarm reaction," and points out that part of this reaction is an enlargement of the cortex of the adrenal gland.

An aspect of the compensation to injury, encountered both in the human being and experimental animals, is a sustained rise in blood sugar in spite of fasting. There is apparently an increased production of glucose from noncarbohydrate sources as well as from glycogen. In human beings following a burn, such a rise in blood sugar occurs. There is also an increased excretion of nitrogen and 17-ketosteroids† in the urine; and it has been postulated that these three findings are signs of augmented activity of the adrenal cortex, part of an "alarm reaction."

Several laboratories have observed an increased renal excretion of nitrogen in the human being following a burn.^{2, 3, 4} The amount of nitrogen may be considerable, indeed, comparable to that encountered in diabetic acidosis. In this latter disease it is believed that there is an overproduction of glucose and ketone bodies from protein; this excessive conversion of protein is perhaps motivated by the anterior pituitary, uninhibited by an adequate supply of insulin. In the burned patient it has been postulated that the excessive nitrogen excretion is the result of increased conversion of protein to sugar, but motivated in this case by the adrenal cortex.^{3, 5}

Long⁶ has produced evidence in experimental animals that the adrenal

* The work described in this paper was done under a contract, recommended by the Committee on Medical Research, between the Office of Scientific Research and Development and Harvard University.

† The term "17-ketosteroid" is applied to those organic compounds which have a ketonic radical attached to the 17-carbon atom of a phenanthrenecyclopentane nucleus. Although this nucleus is common to such sterols as cholesterol, the sex hormones, the adrenal cortical hormones so far identified and members of the vitamin D group, the 17-ketosteroids which are excreted in the urine appear to represent, for the most part metabolic end-products of the androgenic hormones. These end-products originate both in the testis and the adrenal cortex of both sexes. They do not represent, apparently, the entire biologically active secretion of the adrenal cortex. The non-17-ketosteroid excretion product of the adrenal cortical secretion, the so-called "cortin-like" sterols, can be measured only by a difficult biologic assay. The 17-ketosteroids, on the other hand, are determined in the urine by a quantitative colorimetric method and, even though in the male it registers the function of two glands, it is clinically the most useful method available by which adrenal cortical function may be estimated.

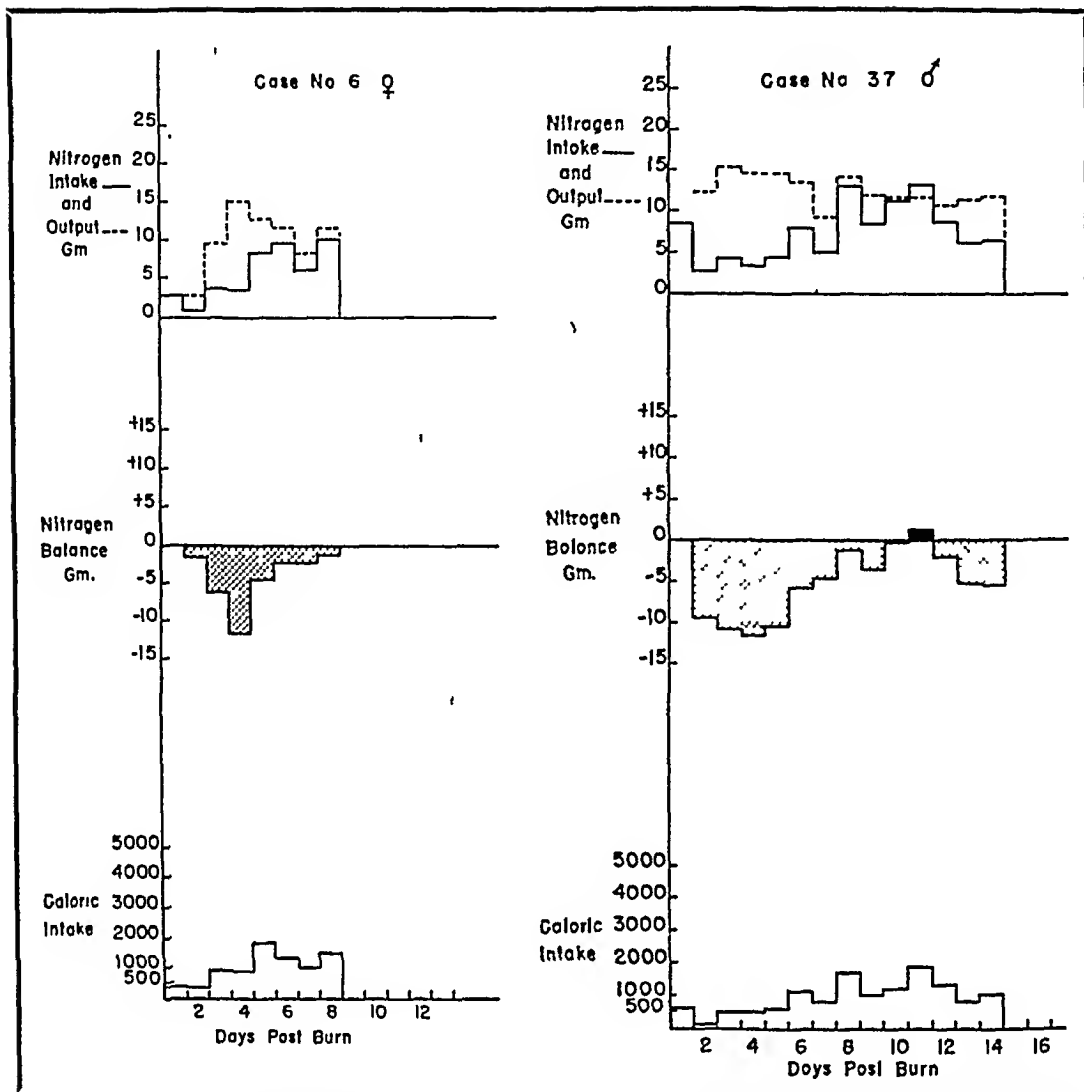
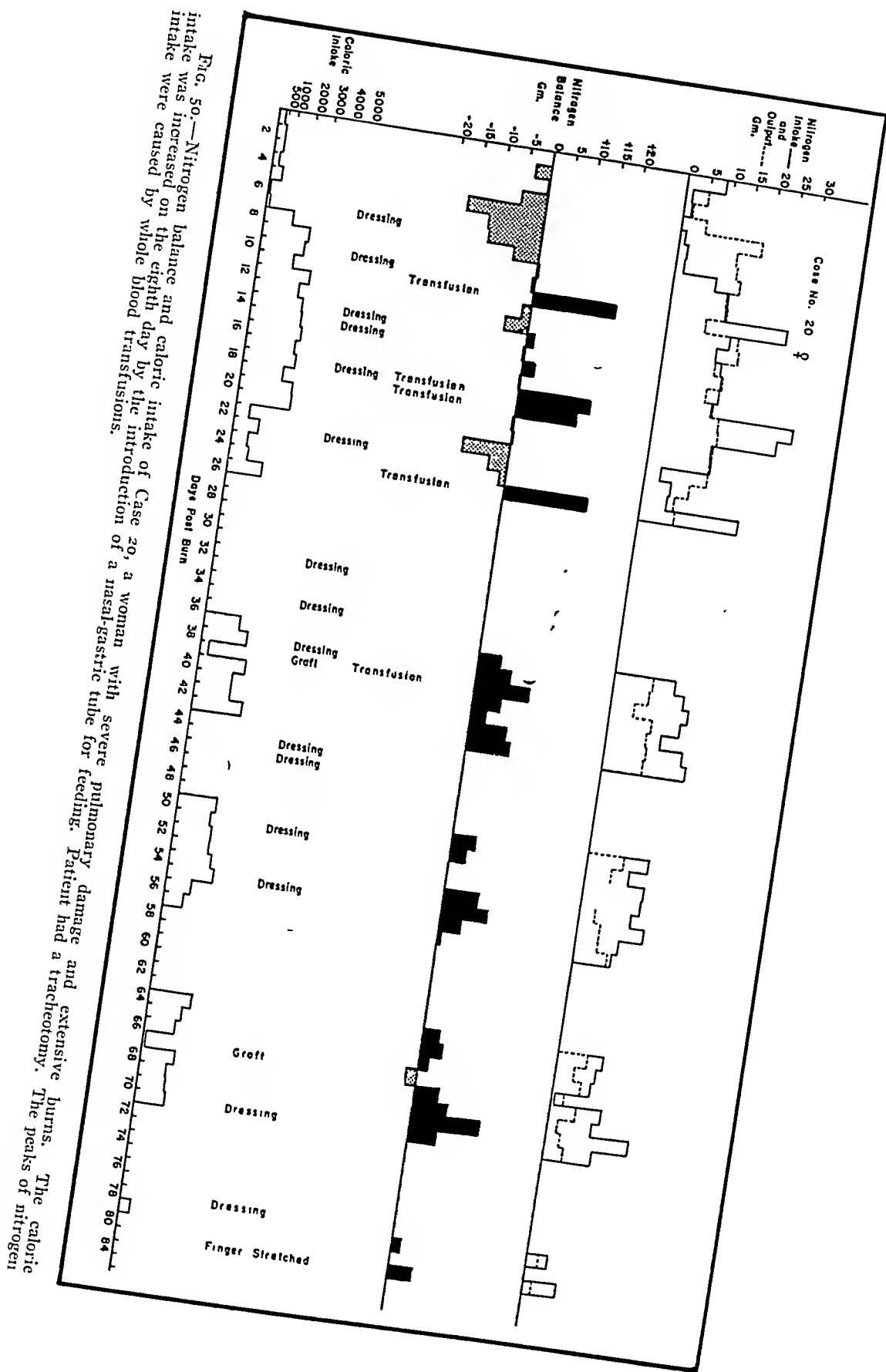


FIG 48—Nitrogen balance and caloric intake of Case 6, a girl with pulmonary damage and no surface burns. She required oxygen therapy for five days. She was afebrile throughout. One unit of plasma was given on the first day.

FIG 49—Nitrogen balance and caloric intake of Case 37, a man with moderate pulmonary damage and mild burns. He received four units of plasma in the first 48 hours.

cortex does activate such a conversion. Whether overactivity of the adrenal is responsible in shock in the human being for an increased production of sugar is not yet established. The observed increased excretion of 17-ketosteroids through the kidney following a burn or other trauma is in keeping with the concept of increased activity of the adrenal cortex.^{3, 5, 7} The relation of the 17-ketosteroids to protein and carbohydrate metabolism appears to us to be still unsettled. Testosterone, which is the secretion of the interstitial cells of the testis and the end-product of which is excreted in the urine as a 17-ketosteroid, causes a retention of nitrogen when injected into a eunuch or a normal man or woman.⁸ Such action on nitrogen balance is the reverse of a conversion of protein to glucose. If the adrenal cortex also secretes steroids which are excreted in the urine as 17-ketosteroids, is the action of these adrenal steroids like that of testosterone?

METABOLIC OBSERVATIONS



It is probable that the cortex of the adrenal is also a source of 17-ketosteroids. This is based on several clinical observations: First, these steroids are found in the urine of both man and woman; there is more in man than woman, but the difference disappears if the man is castrated.⁹ Second, there is a diminished excretion of these steroids in the urine of patients with Addison's disease; in women with this disease there may be little or none.¹⁰ (In Addison's disease, spontaneous hypoglycemia is sometimes encountered indicating an inadequate conversion of noncarbohydrate substances to glucose). Third, patients with a functioning tumor of the adrenal cortex excrete an increased amount of 17-ketosteroids. Removal of the tumor is followed by an abrupt drop in the amount excreted. (Some of the patients in the presence of the tumor have an elevated blood glucose with sugar in the urine, intimating an increased production of glucose from non-carbohydrate sources).

The theories regarding 17-ketosteroids and the adrenal cortex have been further complicated by the suggestion that the cortex secretes two types of hormones. One is a testosterone-like hormone, or "N" hormone, which causes retention of nitrogen, while the other, the "S" hormone, causes conversion of protein to sugar and, therefore, a loss of nitrogen.^{3, 5, 11} The "N" hormone is supposedly excreted in the urine as a 17-ketosteroid, while the "S" is not and is determined only on biologic assay. In the burned patient it is suggested that the adrenal cortex at first puts out an excess of both "N" and "S" hormones but later only the "S"; further, that a subsequently diminished output of "N" hormone, recorded as a decreased 17-ketosteroid excretion, represents a phase deleterious to wound healing, and that injection of testosterone might be beneficial.⁵

Such conflicting theories suggest premises based upon inadequate observations. It is possible that the chemical test which identifies the 17-ketosteroids is measuring steroids with differing physiologic properties. Investigation is needed.

Another problem is that of the source of the increased nitrogen excreted following the burn. It has been held that the nitrogen comes from the burned cells. It might, however, come from the plasma protein or some other noncellular storehouse of nitrogen. In the previous article on the care of shock, the possibility is discussed that the plasma proteins, which have seeped out into the extracellular spaces of the burned area, are excreted by the kidney when resorbed through the lymphatics into the general circulation. It is possible that these proteins are in some way denatured and are, therefore, no longer utilizable by the body when resorbed. Since the protein concentration of the edema fluid of the burned area is high owing to the abnormal capillary permeability induced by the burn, the excretion of such protein would mean a considerable loss of nitrogen.

If the increased nitrogen excreted comes from cells, there should be a parallel excretion of other substances contained in cells, such as potassium and phosphate. If it comes from plasma protein, these cellular parallels

METABOLIC OBSERVATIONS

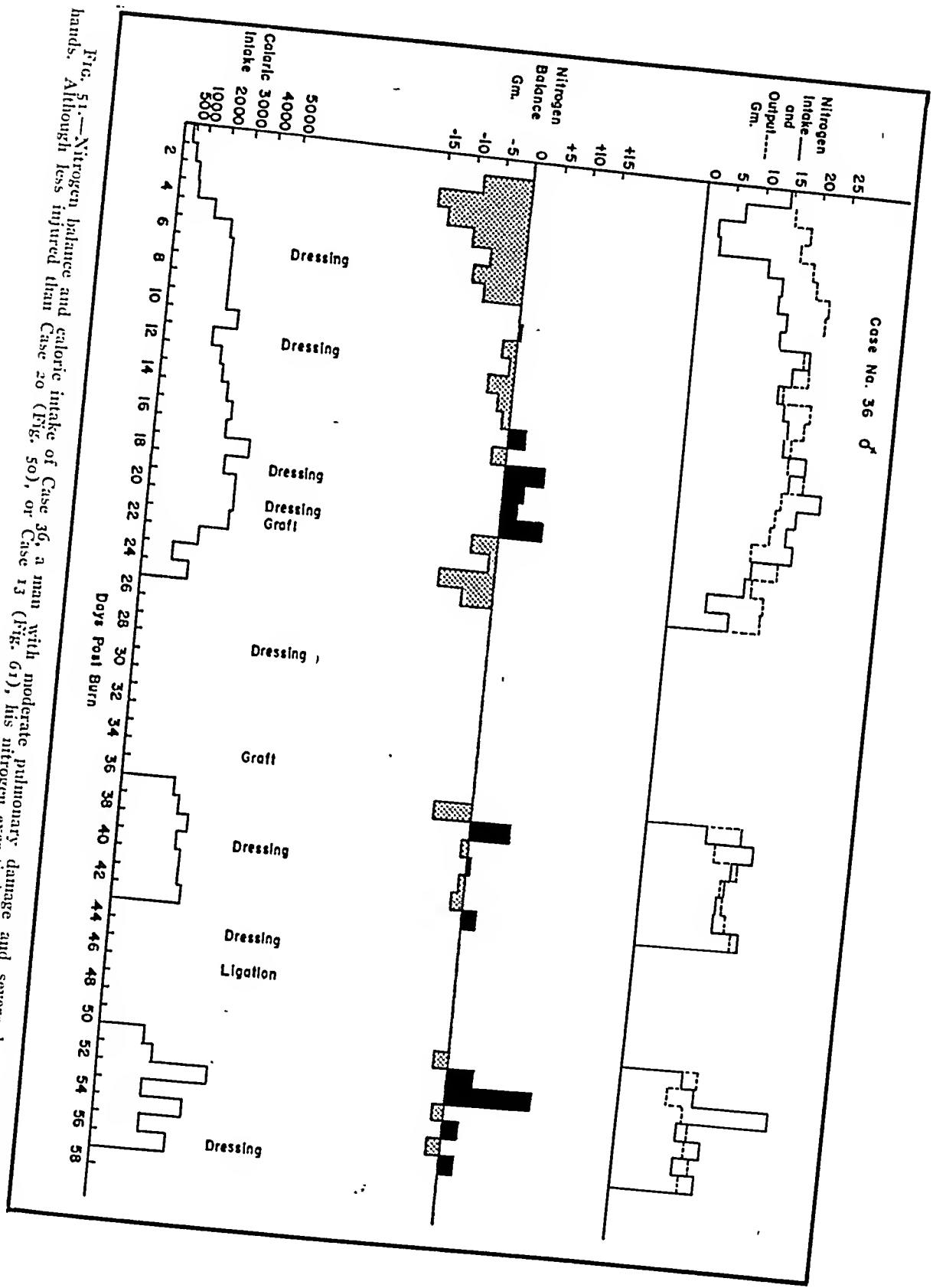


Fig. 51.—Nitrogen balance and caloric intake of Case 36, a man with moderate pulmonary damage and severe burns of head and hands. Although less injured than Case 20 (Fig. 50), or Case 13 (Fig. 61), his nitrogen excretion was greater.

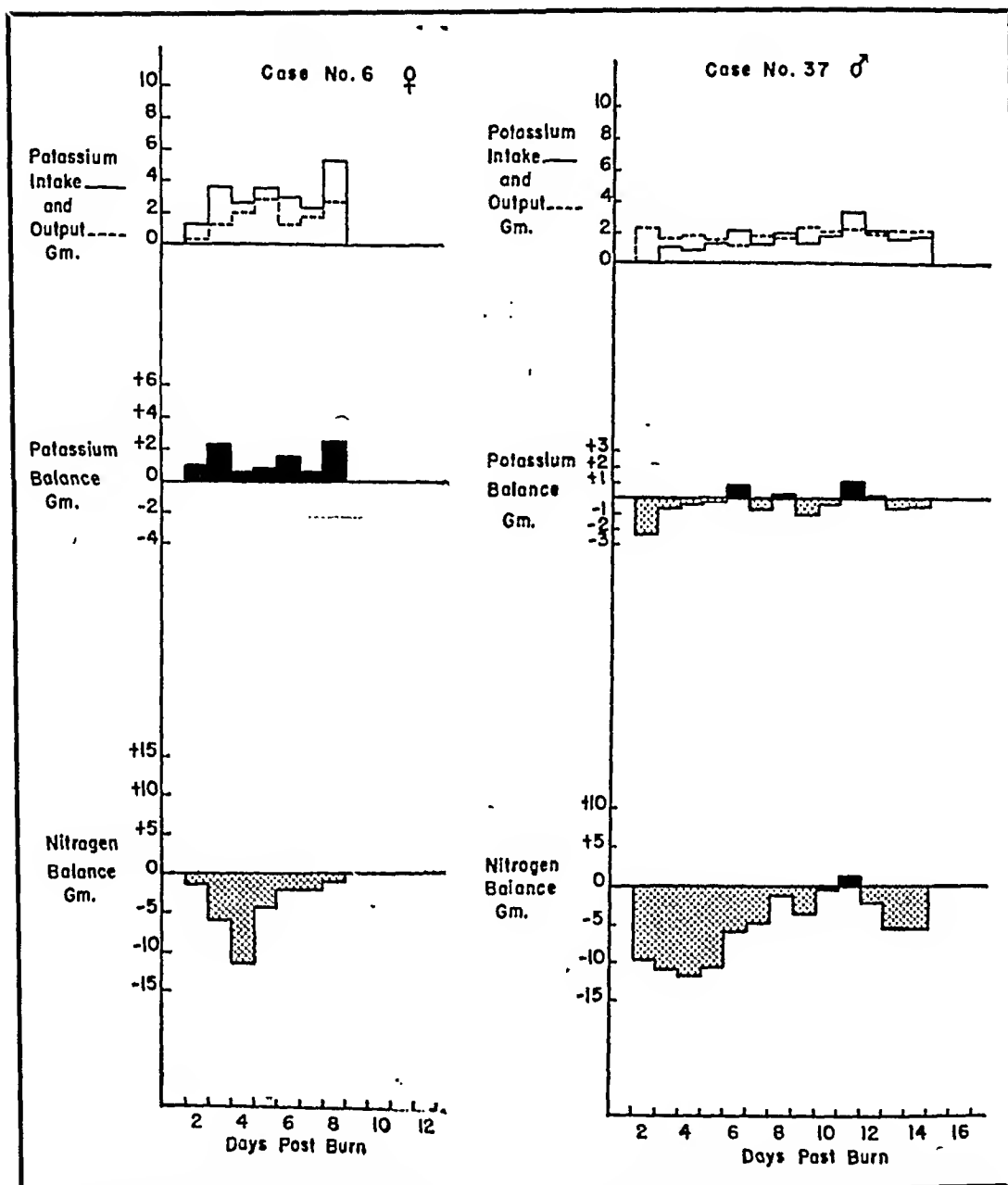


FIG. 52.—Potassium balance, with nitrogen balance curve for comparison, in Case 6 (same case as Figures 48 and 57).

FIG. 53.—Potassium balance, with nitrogen balance curve for comparison, in Case 37 (same case as Figures 49 and 58).

would be missing. As far as we are aware, no studies of potassium and phosphate balance have been made in patients following burns.

In view of the conflicting evidence regarding the adrenal cortex and shock, it was decided to study in human burn shock the relations of 17-ketosteroid excretion to nitrogen metabolism, and of nitrogen to cellular metabolism.

EXPERIMENTS

Various aspects of metabolism were studied in 29 of the 39 victims of the Coconut Grove fire treated at the Massachusetts General Hospital.

METABOLIC OBSERVATIONS

Twenty-four-hour urine specimens were collected on all these patients. Some specimens were not complete, particularly in the first 72 hours, when a few patients were incontinent. At times urine was lost with the stool, and an occasional specimen was inadvertently thrown away.

Nitrogen Balance.—The nitrogen excretion in the urine was measured throughout their stay in the hospital. An accurately recorded intake of food is available for only nine of these patients throughout their hospital stay, and in these nine only, therefore, is a complete nitrogen balance available.* In five more patients food intakes were adequately recorded over considerable periods, and the nitrogen balance has been calculated for these periods. On the remaining 15 patients, only the outputs are available.

Smaller negative balances were encountered than anticipated. Of the nine patients with complete balances, two died within the first 72 hours, one having been in slight positive, the other in slight negative balance. Of the seven survivors with complete balances, two were in positive balance from the beginning owing in part to transfusions. One of these was the most severely burned of the 39 patients (Case 13. See Fig. 61). Twenty-eight per cent of the body was third degree burn and required grafting, another 28 per cent was second degree, making a total of 56 per cent of the body surface being severely burned, with an unknown quantity of first degree burn (see colored section, Fig. 11). The other patient (Case 32) was also in positive balance owing to multiple transfusions given early to relieve anoxia.

The remaining five patients with complete balances showed negative balances up to nine days. During this period of negative balance, the caloric intake of the patients was inadequate for maintenance. It is believed that negative balance is in large part accounted for by the low caloric and low protein intakes. The nitrogen data of four of these patients, together with the caloric intakes, are shown in Figures 48-51. An increased intake of protein apparently did not alter the nitrogen excretion.

In the five patients with incomplete balances, as well as in the 15 with nitrogen excretions only, the pattern of urinary nitrogen excretion is the same as in those with complete balances. (The nitrogen data of the final patient with complete, and two with incomplete balances are shown in Figures 59, 60 and 63.) Of interest in all of the 29 patients in whom the nitrogen excretion was determined, is the constancy of the level of

* The balance figures are constructed on the basis of the calculated nitrogen intake by mouth and by vein, against the nitrogen excretion in the urine. No attempt was made to measure the loss of nitrogen from the wound, that is, by leakage of the protein-rich fluid into the bandages. Nor was the increased nitrogen of certain stools measured. Ordinarily the stools contain approximately 10 per cent of the total nitrogen excreted, but in those containing blood there was, of course, additional nitrogen lost. (Five of the nine patients had stools positive to guaiac on one to three occasions in the first two weeks; there was no gross bleeding.)

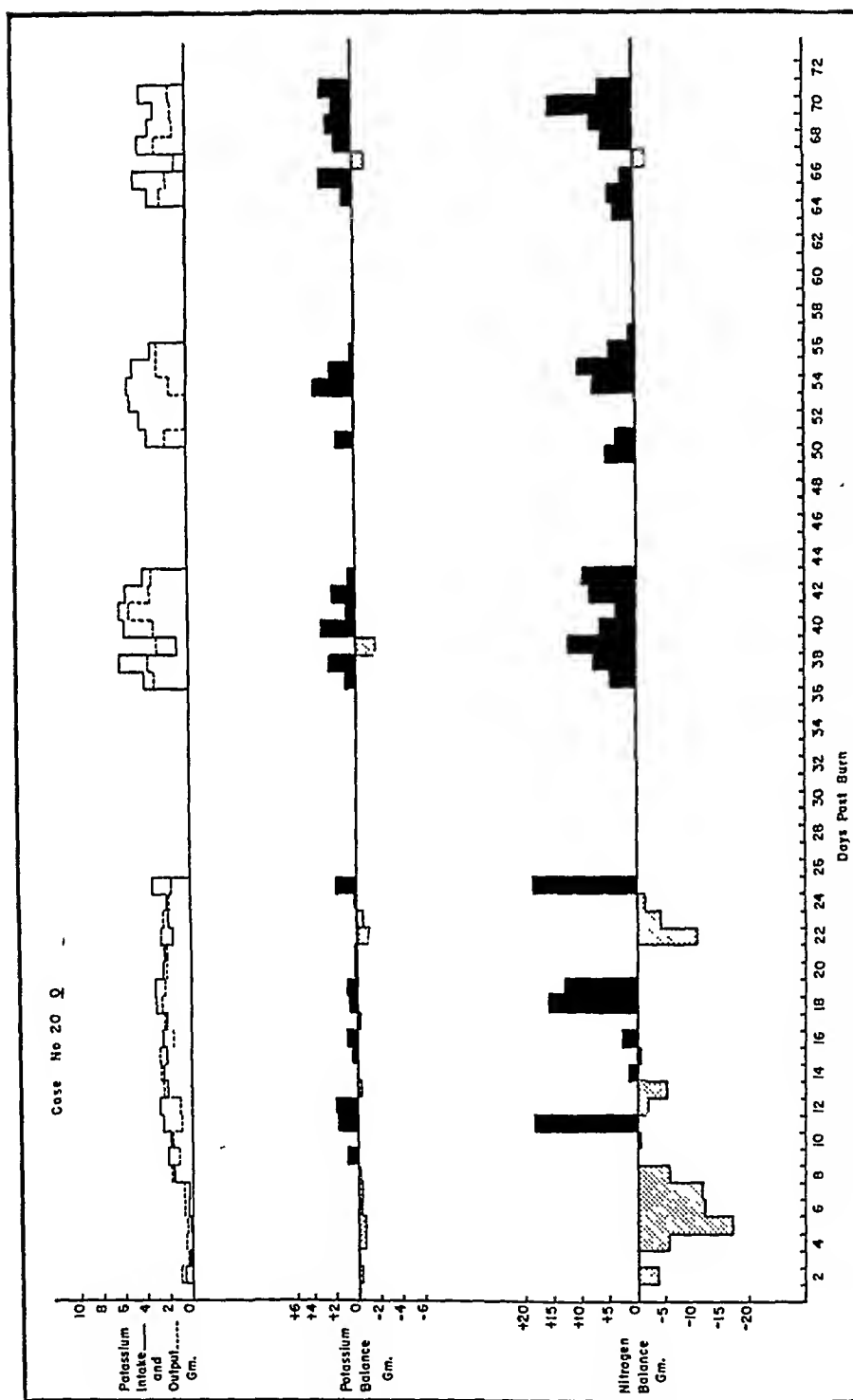


Fig. 54.—Potassium balance, with nitrogen balance curve for comparison in Case 20 (same case as Figures 50 and 62).

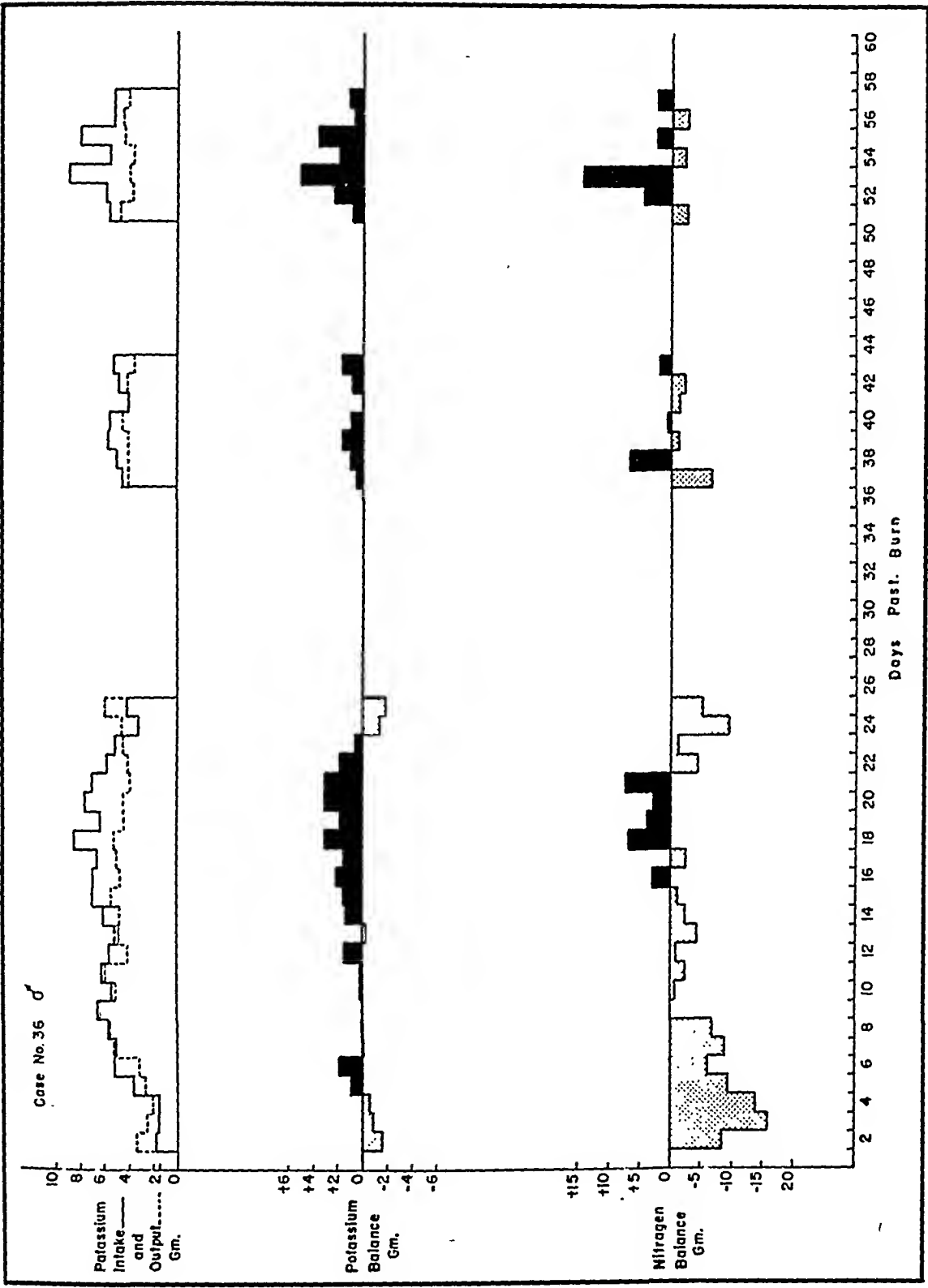


Fig. 55.—Potassium balance, with nitrogen balance curve for comparison in Case 36 (same case as Figures 51 and 64).

excretion. It is a little higher during the first week, generally, than in later weeks.

The level of nitrogen excretion was higher in the males than in the females. This is in keeping with the differences in size and caloric requirements of the sexes. The extent of the skin burns did not influence the level of nitrogen excretion in either sex. Thus, of the four males with complete nitrogen balances, Case 37, with minor burns, showed the lowest excretion; Case 11, with the most extensive burns, and Case 29, with moderate burns, were in the middle, and Case 36, also with moderate burns, was highest. Cases 29 and 36 had almost identical anatomic areas involved, but the burns of Case 36 showed more infective organisms, and the initial grafts failed, in part, to survive.

Potassium Balance.—Potassium balances were measured in six of the seven surviving patients with the complete nitrogen balance (Figs. 52-55). The patients were essentially in potassium balance throughout, but all exceptions should be mentioned. Case 37 (see Fig. 6) on the second day was in negative balance. In the two patients whose potassium balance charts are not shown (Cases 13 and 32), there was a positive potassium balance which was presumably due to the whole blood transfusions which these patients received.

The absence of a negative potassium balance, with the one exception noted, suggests that the nitrogen excreted in excess of the intake in the early days did not occur as a result of cell destruction.

Calcium and Phosphorus Excretion.—The excretion of calcium and phosphorus was measured in the urine of one patient (Case 36), (see Fig. 56). In view of the calculated intakes of these two substances in the diet, the output of both is within the expected level of normal. The fecal calciums were not measured, so a complete balance was not determined. The injury, or the rest in bed, was without apparent effect on the urinary excretion of these substances.

17-Ketosteroid Excretion.—The urinary excretion of 17-ketosteroids has been measured in 23 patients. The method of determination is described elsewhere.^{12, 13} The determinations were continued throughout the hospital stay, and in some instances after discharge. During the first week, assays were carried out daily, and thereafter at intervals of two to three days.

The data of eight typical patients are presented in Figures 57-64. The selection of the patients for illustration was based primarily on the length of the study and the severity of the injury which they had received. All had nitrogen and six had potassium studies in addition.*

* Normal values for 17-ketosteroids in this laboratory range between 6 to 15 mg. per 24 hours in females, whereas, the range in the male is from 10 to 20 mg. Values at either extreme are unusual in our experience. In the same normal individual the daily fluctuations are not more than 25 per cent from the average of consecutive assays, and frequently are much less. Hence, marked variations in output are considered significant.

METABOLIC OBSERVATIONS

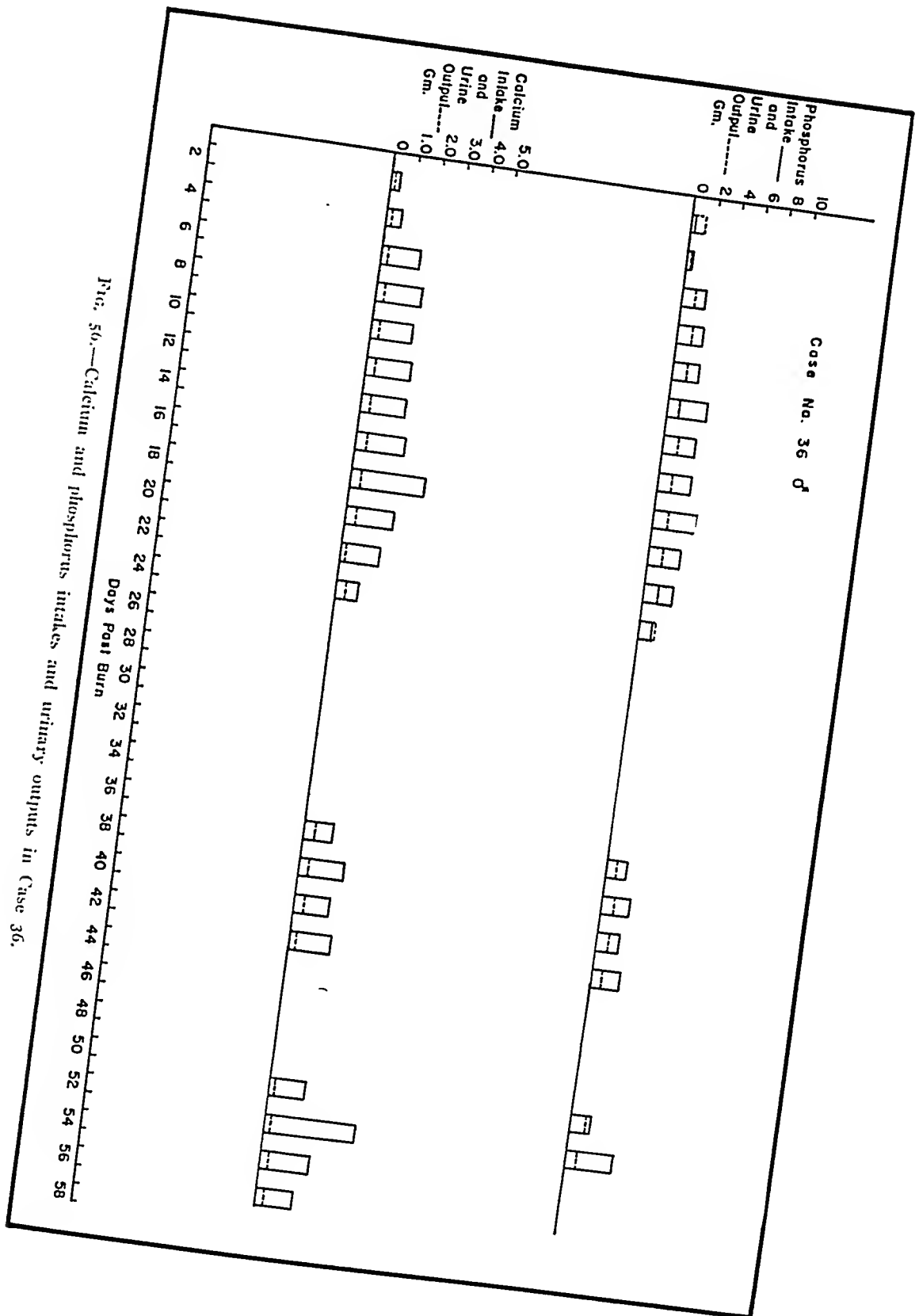


FIG. 56.—Calcium and phosphorus intakes and urinary outputs in Case 36.

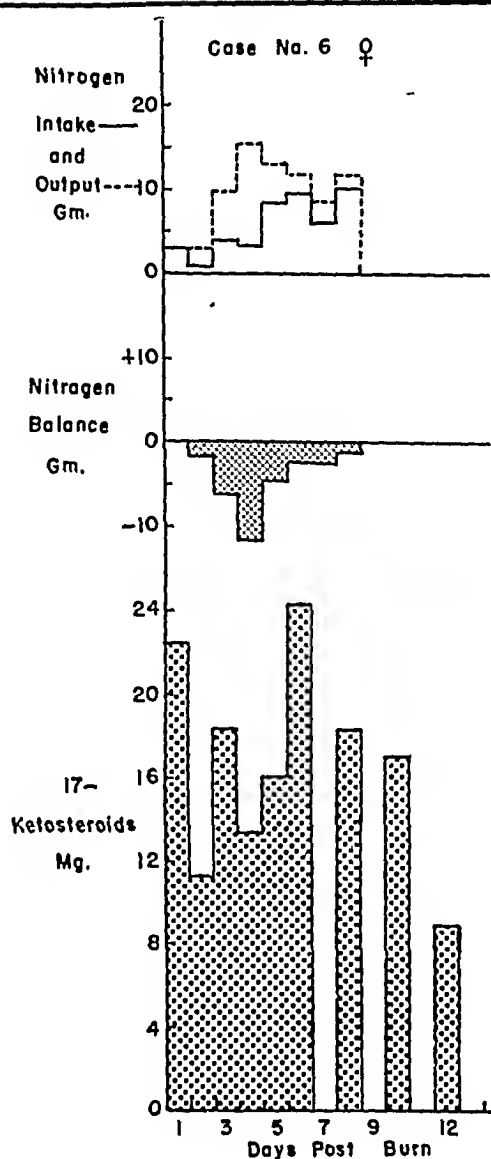


FIG. 57.—17-ketosteroid excretion with nitrogen balance for comparison, in Case 6. (See also Figures 48 and 52.)

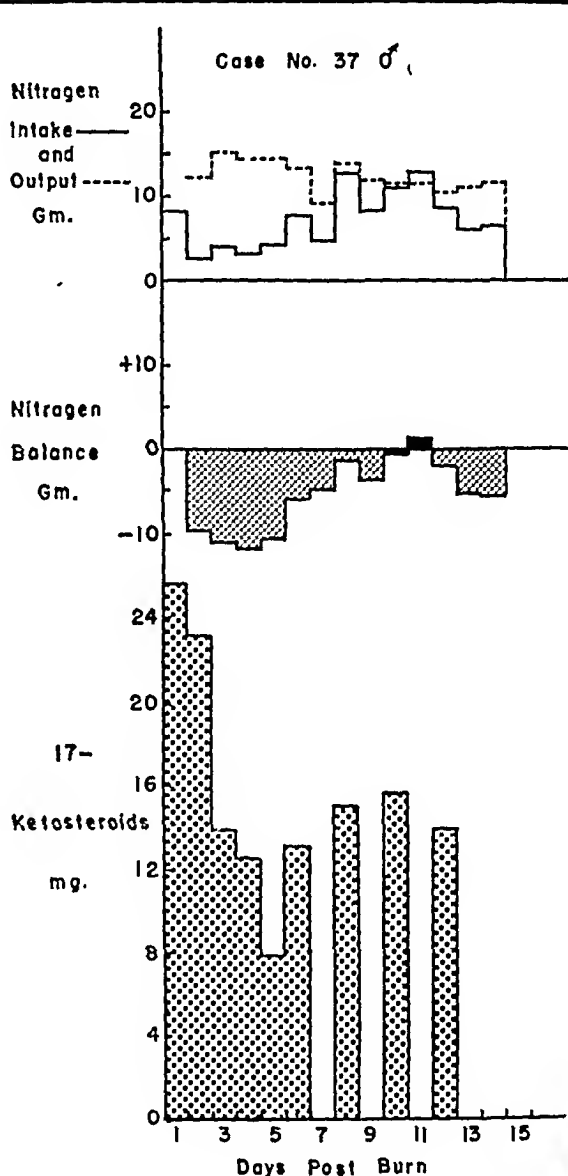


FIG. 58.—17-ketosteroid excretion with nitrogen balance for comparison, in Case 37. (See also Figures 49 and 53.)

The levels of the 17-ketosteroid excretion are all high normal or above normal range for each sex during the first three to seven days after injury. Following this there is a precipitous drop to low normal or subnormal outputs. This decrease was found in all but a few patients who had the mildest injuries, or who were discharged from the hospital before such a drop could have been noted. Thereafter, except for occasional fluctuations, especially in the male patients, the 17-ketosteroid excretion remains at a relatively low level for a long period. In several, a rise to an average normal level did not occur until six weeks had elapsed (Figs. 63 and 64). In others this is not apparent until later (Figs. 60 and 62). In two women the levels are still low 113 days after the injury (Figs. 59 and 61). In general, the

METABOLIC OBSERVATIONS

duration of the low level of 17-ketosteroid excretion correlated closely with the extent of injury and period of convalescence.*

CLINICAL CORRELATIONS

In the six female patients with third degree burns who remained in the hospital for grafting, two observations were made, of interest in view of the metabolic studies.

The catamenia ceased in all six. It returned in one (Case 20) before discharge from the hospital, at the end of two and one-half months. In the next two it returned soon after discharge (Cases 23 and 28). In the remaining three (Cases 2, 8 and 13) it had not returned at four and one-half months.

Increased growth of hair was noted in all six. In five, the growth occurred on the face; in two, there was a thick growth, in one, on the cheeks, and in the other, on the lips, chin and neck. In all six there was an increased growth on the extremities. The patients noticed this growth themselves, and at first were hesitant to mention it. All were gratified to know it was not unexpected and that the others shared in it. With the return of catamenia in one patient, the hair on the legs has already begun to drop out.

The pattern of 17-ketosteroid excretion was typical in all six patients. The increased hair growth occurred when the 17-ketosteroid excretion was low. The hair growth was thickest in two of the patients with the lowest and most prolonged depression of 17-ketosteroid excretion (Figs. 59 and 61). The 17-ketosteroid excretion rose to a normal level at about the time catamenia was resumed in the three patients in whom that has occurred. (One of these was Case 20, Fig. 62).

COMMENT

The level of nitrogen excretion found in these patients was less than was anticipated, and the ease with which nitrogen equilibrium was realized was a surprise. Even in these patients who were severely burned, the loss of nitrogen was no greater than in those with relatively mild injury. The nitrogen balances observed, no matter what the extent of the injury, correlate more closely with the caloric and nitrogen intakes than with other factors. For example, males, with their higher caloric requirement, excreted consistently larger amounts of nitrogen than the females.

The negative nitrogen balances, observed during the periods of inadequate caloric and nitrogen intakes, were not accompanied by a negative potassium balance.

* It is to be noted that in Case 36, Figure 64, the levels are never below normal, but perusal of the data reveals the usual down swing with a typical valley before a rise to higher levels. Following discharge his levels are higher than average normal values. If these are normal for this individual then the lowest values are distinctly subnormal for him.

There was a more consistent daily excretion of 17-ketosteroids in the female than in the male. This may be attributed to additional gonadal activity in the male.

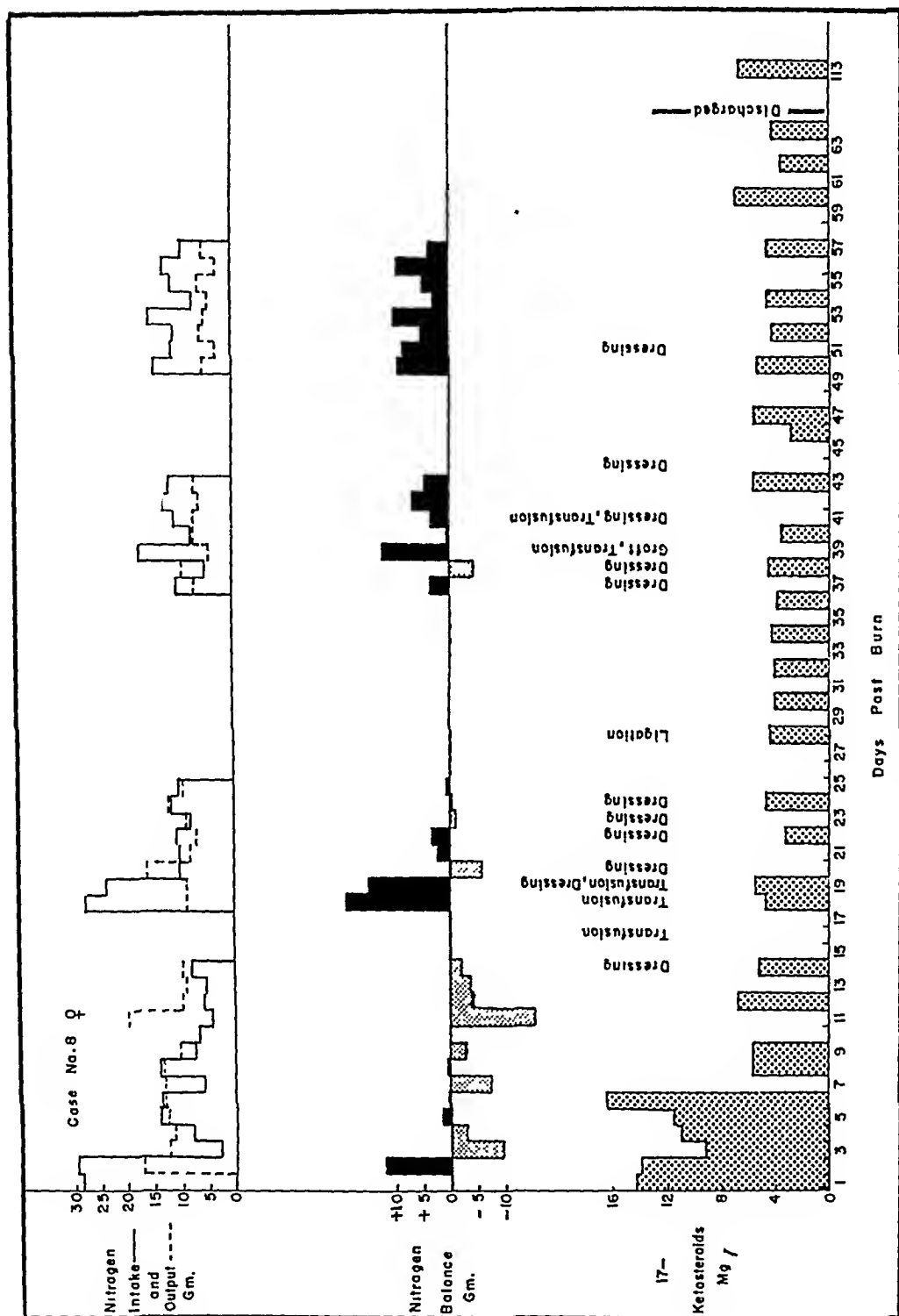


Fig. 59.—17-ketosteroid excretion, with nitrogen balance for comparison, in Case 8, a woman with severe pulmonary damage and moderately extensive burns.

METABOLIC OBSERVATIONS

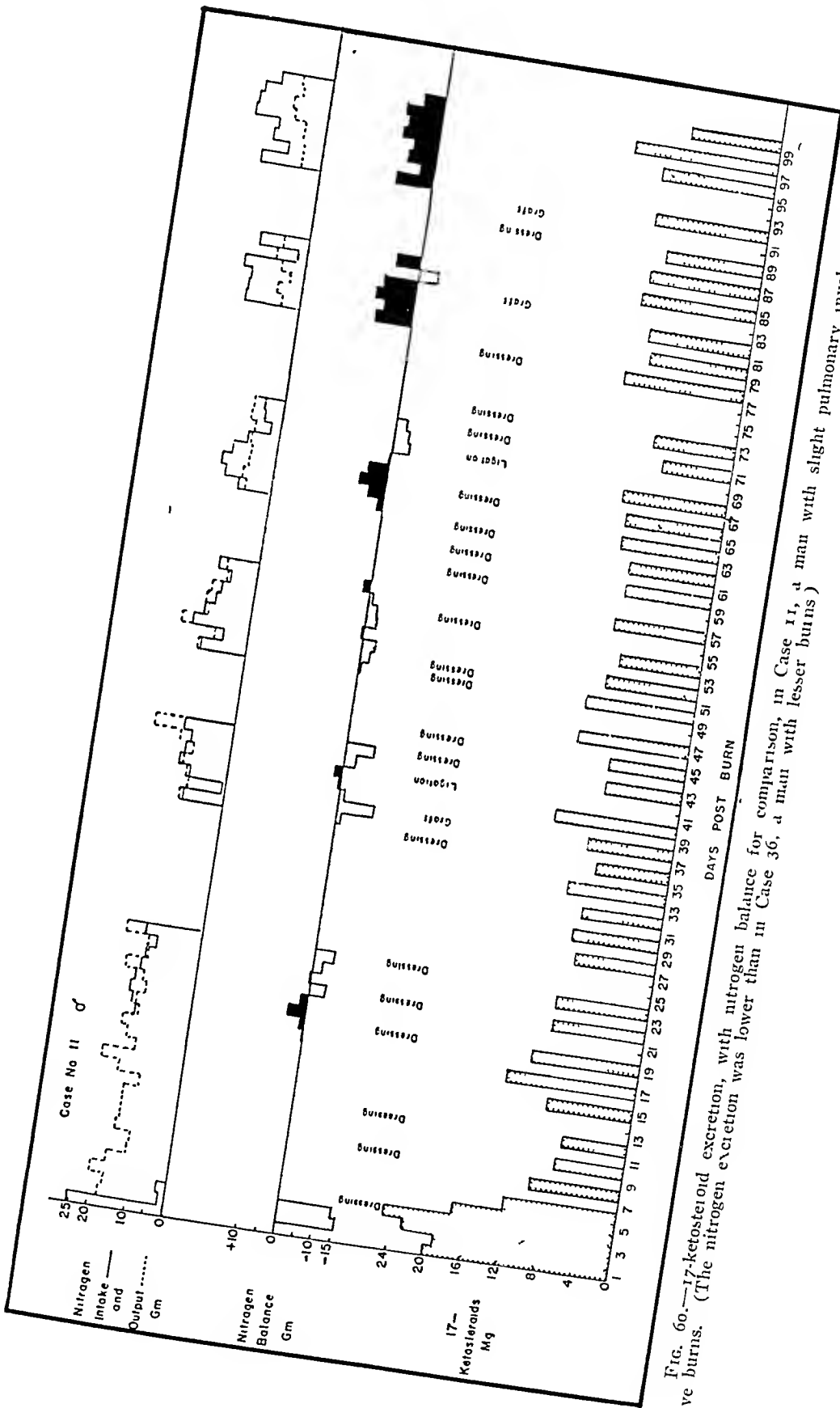


Fig. 60.—17-ketosteroid excretion, with nitrogen balance for comparison, in Case 11, a man with slight pulmonary involvement and extensive burns. (The nitrogen excretion was lower than in Case 36, a man with lesser burns)

balance (with the exception of one day in a single patient). The nitrogen lost, therefore, was presumably not at the expense of cellular protein.

These results are at some variance with what we had been led to expect from the observations of others.^{2, 3, 4} It is obvious that extensive deep burns are not necessarily accompanied by a large loss of nitrogen in the urine. We have, therefore, wondered what factors other than the burn itself might be involved. One thing which was clear, was the absence of invasive infection in the wounds of these patients. Infections such as typhoid or pneumonia cause a loss of nitrogen. At the moment, we ascribe the maintenance of the nitrogen balance of these patients to the relative lack of infection, or, in other words, to the effectiveness of the chemotherapeutic program. Certainly, the simplified method of treating the burned surfaces did not lead to tissue destruction and protein loss. (See article on Surface Treatment).

A factor which has been reported to influence the nitrogen balance is adrenal cortical activity. It is well recognized that the cortex of the adrenal gland is disturbed following severe burns. A patient, studied recently at this hospital, following acid burns, died on the twenty-sixth day of extensive infection. The adrenal cortices were found at postmortem examination to have hypertrophied. On the other hand, acute adrenal cortical necrosis is known to occur, and was observed in two of these patients (Cases 7 and 27) who died on the third day. (See article on Pathology).

It is possible that the changes in 17-ketosteroid excretion observed in these patients reflect alterations in adrenal cortical function. The rise of excretion of these steroids in the first days after the burn would mean an increased activity and the subsequent decline, a depression. It has been suggested that the decline of 17-ketosteroid excretion after injury is due to preferential formation of the "S" hormone by the gland. An increased excretion of cortin-like (non-17-ketosteroid) hormone has been determined by the biologic method.³ The decline in 17-ketosteroids could also be due to inability of the gland to secrete because of either anatomic or physiologic deficiency.

What emerges from the present studies is the constancy of the pattern of 17-ketosteroid excretion which follows this type of injury. In all patients in whom there was more than minimal damage, either in the form of pulmonary inflammation or surface burn, the excretion of 17-ketosteroids in the urine was initially at a high level, almost certainly above normal, to be followed by an abrupt decrease to a low level. This subnormal level remained until the patients had recovered.

This pattern does not follow all injuries or burns. For example, the 17-ketosteroid excretion of the patient mentioned who was found to have hypertrophy of the adrenal cortex following acid burns, showed normal levels throughout the 26 days of his survival. It is possible that other patterns will be found. It should also be pointed out that the urinary 17-ketosteroids represent only excretory products and that these may not be a direct index of secretion or utilization of the precursor. At the present time, all that can



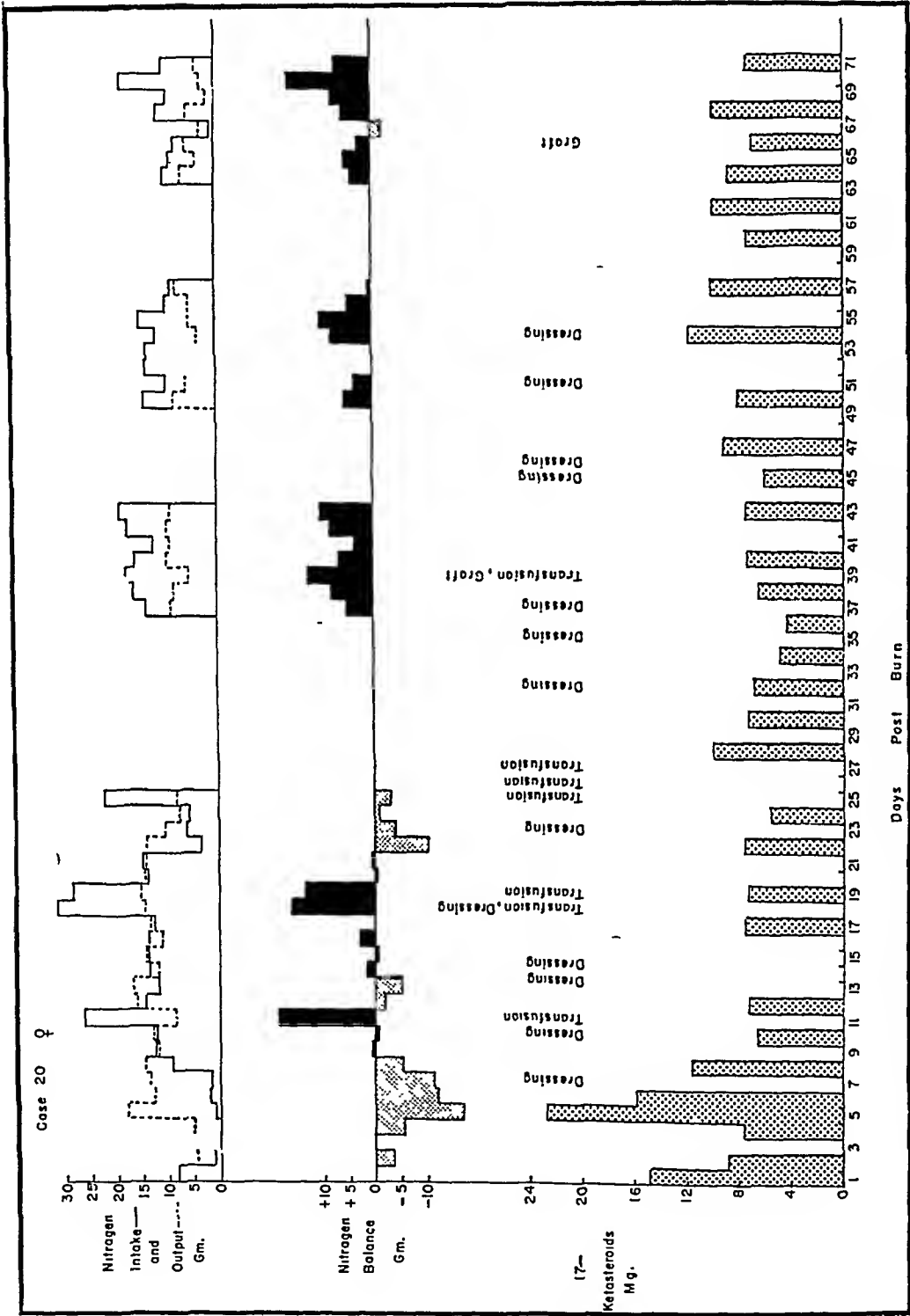


Fig. 62.—17-ketosteroid excretion, with nitrogen balance for comparison, in Case 20. (See also Figures 50 and 54.)

be said is that the relation of 17-ketosteroids to adrenal cortical function and the relation of both to nitrogen metabolism have not been settled.

Amenorrhea in the female patients was expected, but hirsutism in the presence of a low 17-ketosteroid excretion was not. Ordinarily, women with hirsutism have an excretion level at least in the upper limits of normal, if not elevated, as in those with true virilism due to tumor.¹⁴ There are two possible explanations: Either utilization of masculinizing hormone was increased in these patients; or the activity of the hormone present was uninhibited by a relatively low concentration of ovarian hormone. A situation similar to this latter possibility exists frequently after the spontaneous menopause or after castration.¹⁴

No evidence was disclosed suggesting that the administration of testosterone would be beneficial to patients following burns *per se*. Nitrogen equilibrium was obtained readily without it, even in the severely burned. The greater growth of abnormal hair, which presumably would have occurred had testosterone been injected, would have represented a further androgenic-estrogenic glandular imbalance. It is still theoretically possible that in patients depleted by prolonged sepsis and malnutrition, with specific testicular and adrenal cortical insufficiencies, testosterone therapy might be indicated. In like manner adrenal cortical therapy might prove useful.

SUMMARY AND CONCLUSIONS

Metabolic studies were carried out on 29 of the 39 victims of the Coconut Grove disaster treated at the Massachusetts General Hospital. A complete nitrogen balance was obtained in nine patients, and a potassium balance in six of these. The excretion of 17-ketosteroids in the urine was measured in 23 patients. In one the calcium and phosphorus excretion was determined.

In many patients, in the first week, there was a moderate negative nitrogen balance. For the same periods in these patients there was a caloric intake inadequate for maintenance. Nitrogen equilibrium was easily established when the caloric and nitrogen intakes were increased. The level of nitrogen excretion was fairly constant from day to day and was not altered by a rising protein intake; it was, however, less in later weeks than during the first week.

The level of nitrogen excretion bore no relation to the severity of the burn, but males excreted more than females. It is believed that the moderate nitrogen loss encountered was due to the relative absence of invasive infection.

Potassium equilibrium was maintained. The source, therefore, of the nitrogen lost during the period of negative nitrogen balance was non-cellular protein.

The 17-ketosteroid excretion was elevated during a period corresponding to the negative nitrogen balance. After this first week it fell off abruptly to a low level. During this period the nitrogen excretion, however, did not change. The eventual return of the 17-ketosteroid excretion to normal was

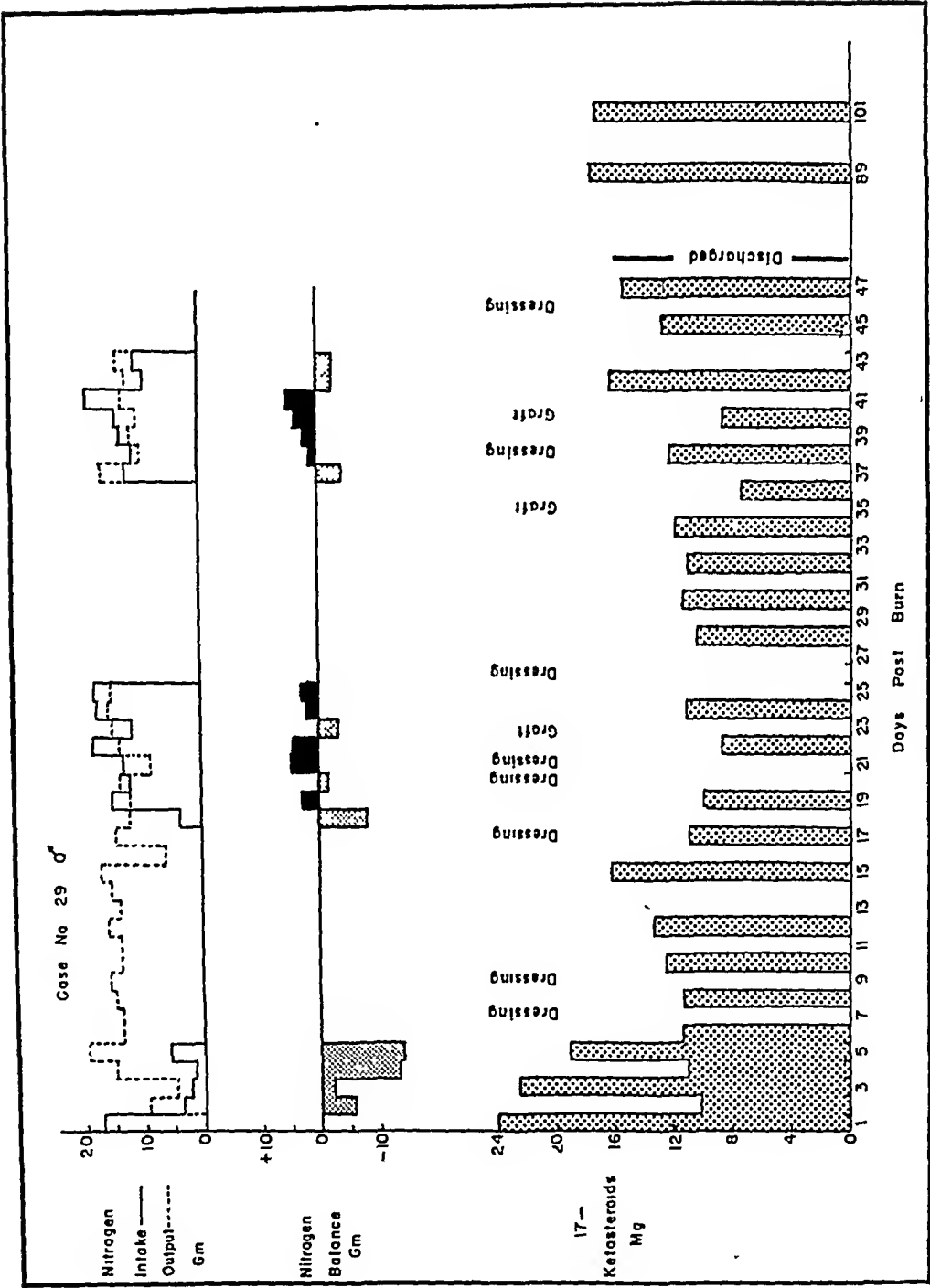


FIG. 63.—17-ketosteroid excretion, with nitrogen balance for comparison, in Case 29, a man with moderate pulmonary damage and severe burns of head and hands, comparable to Case 36.

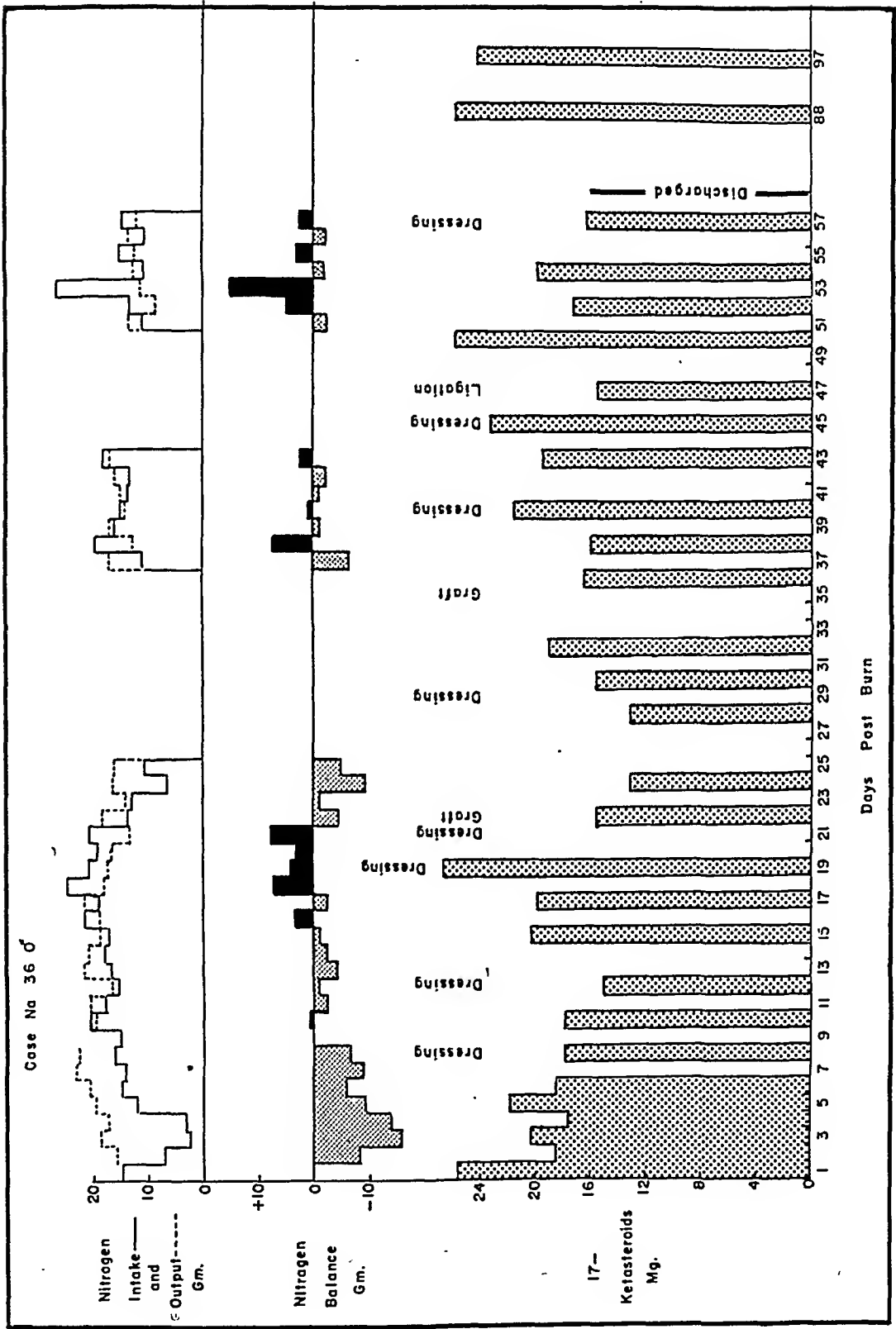


Fig. 64.—17-ketosteroid excretion, with nitrogen balance for comparison, in Case 36. (See also Figures 51, 55 and 56.)

simultaneous with the return to good health. The relation of the 17-ketosteroid excretion to nitrogen metabolism and to adrenal cortical activity was not settled.

An abnormal growth of hair was encountered in the six women hospitalized for more than three weeks, despite the low 17-ketosteroid excretion levels.

The ease with which nitrogen equilibrium was obtained, and the abnormal hair growth in the women, do not suggest testosterone as a routine therapy for patients following burns.

REFERENCES

- ¹ Selye, H.: Studies on Adaptation. *Endocrinology*, **21**, 169, 1937.
- ² Lucido, J.: Metabolic and Blood Chemical Changes in a Severe Burn. *ANNALS OF SURGERY*, **111**, 640, 1940.
- ³ Browne, J. S. L.: Personal communication: Conference on Bone and Wound Healing, December 11-12, 1942. Published by Josiah Macy, Jr., Foundation, New York, N. Y.
- ⁴ Taylor, F. H. L.: Personal communication.
- ⁵ Albright, F.: Personal communication: Conference on Bone and Wound Healing, December 11-12, 1942. Published by Josiah Macy, Jr., Foundation, New York, N. Y.
- ⁶ Long, C. N. H.: A Discussion of the Mechanism of Action of Adrenal Cortical Hormones on Carbohydrate and Protein Metabolism. *Endocrinology*, **30**, 870, 1942.
- ⁷ Forbes, A. P.: 17-Ketosteroid Excretion in Stress: Preliminary Report. Limited publication by Josiah Macy, Jr., Foundation, New York, N. Y., 1942.
- ⁸ Knowlton, K., Kenyon, A. T., Sandiford, L., Lotwin, G., Fricker, R.: Comparative Study of Metabolic Effects of Estradiol Benzoate and Testosterone Propionate in Man. *J. Clin. Endocrinology*, **2**, 671, 1942.
- ⁹ Scott, W. W., and Vermeulen, C.: Studies on Prostatic Cancer: Excretion of 17-Ketosteroids, Estrogens and Gonadotropins before and after Castration. *J. Clin. Endocrinology*, **2**, 450, 1942.
- ¹⁰ Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H., and Reifenshtein, E. C., Jr.: Colorimetric Assay of 17-Ketosteroids in Urine. *J. Clin. Endocrinology*, **1**, 234, 1941.
- ¹¹ Albright, F., Smith, P. H., and Fraser, R. W.: A Syndrome Characterized by Primary Ovarian Insufficiency and Decreased Stature. *Am. J. M. Sci.*, **204**, 625, 1942.
- ¹² Nathanson, I. T., Towne, L. E., and Aub, J. C.: Normal Excretion of Sex Hormones in Childhood. *Endocrinology*, **28**, 851, 1941.
- ¹³ Nathanson, I. T., and Wilson, H.: Factors Affecting Colorimetric Urinary Ketosteroid Determinations. *Endocrinology*, in press.
- ¹⁴ Nathanson, I. T.: Unpublished data.

PROTOCOLS

The extent of the surface burns as recorded in the protocols is based on observations at the time of the first change of dressing (five to ten days after injury). Therefore, the extent of the first degree burns could not be ascertained except of the face, where there was obvious edema and no tissue destruction. The percentages are calculated on the basis of first, second and third degree burns of the face, and of second and third degree burns of the rest of the body surface. The Berkay scale was used.

Case 1.—Male, age 27. In trying to crawl out of the burning building, the patient felt the flames shooting up his back and over his face and believes that he breathed flames. He lost consciousness on reaching a door.

Condition on Arrival: He was conscious, not in shock, had slight cherry color of mucous membranes, and râles on auscultation of the chest.

Extent of Burn: First degree: Face. Second degree: Hands, back, thighs, legs. Third degree: Back. Total: 15.5%. Corneal and inhalation burns present.

Plasma Therapy: None. **Blood Pressure:** Remained normal. **Laboratory Data:** Maximum hematocrit was 52% at 31 hours; blood potassium 3.9 m.Eq. on second day; all other determinations also normal.

Clinical Course: The burned areas did not require grafting. **Pulmonary Complication:** Patient developed moderate respiratory difficulty, with some cough and expectoration. Chest roentgenograms, however, were negative and the respiratory difficulty cleared before discharge. **Subsequent Transfusions:** None.

Chemotherapy: Sulfadiazine was continued until the twenty-sixth day. **Penicillin:** None. **Operations:** None.

Discharge: On twenty-sixth day, with one small granulating area on back and one on leg; subsequently healed. No respiratory difficulty.

Case 2.—Female, age 38. Patient was in lobby, saw man rush up stairs with clothes on fire. She was 10 feet from revolving door at entrance, was swept toward it by rush. Remembers choking, lost consciousness at revolving door.

Condition on Arrival: Patient was hysterical, manic and in great pain. She was not in shock. Mucous membranes were cherry-red color.

Extent of Burns: Second degree: Face, scalp, hand, thighs, legs. Third degree: Hand, wrist, scalp. Total: 17.5%. Inhalation burns. (See color section, Figs. 13 and 14).

Plasma Therapy: Two units in first 24 hours. **Blood Pressure:** Seventy systolic soon after admission, gradually rose during the first 24 hours. **Laboratory Data:** Maximum hematocrit was 51% at 37 hours. Had sulfadiazine level of 7.4 mg. 12 hours after burn. Slowly developed an anemia, with hematocrit of 34% on fifty-first day. Blood potassium was 3.4 m.Eq. on first day and 4.0 m.Eq. on second day. All other determinations normal.

Clinical Course: The burned areas were grafted with satisfactory results. Abnormal growth of hair occurred on face and forearms. Catamenia absent. **Pulmonary Complication:** Patient had received 3/4 gr. morphine subcutaneously on entry, and was almost apneic on reaching the ward. Respiratory respiration, with oxygen through an intratracheal tube, was carried on for five hours. Developed auricular fibrillation which lasted for 24 hours; probable cause was anoxia. The patient was digitalized and oxygen therapy, using a tent, was continued for five days. The patient's respiratory difficulty with cough and some sputum continued for about six weeks, gradually clearing.

Because of the possibility that the subsequent chest lesions were pulmonary infarcts, bilateral superficial femoral vein ligation was carried out on the fifty-second day. **Subsequent Transfusions:** Two whole blood.

Chemotherapy: Sulfadiazine continued until seventeenth day. **Penicillin** from sixth to twenty-ninth day. **Operations:** Plastic to left hand, abdominal flap, skin graft to wrist on twenty-eighth day. Partial section of flap on forty-second day. Plastic to left hand, abdominal flap detached on forty-eighth day. Bilateral superficial femoral vein ligation on fifty-second day, no clot found. Graft of abdominal wall defect on seventieth day. **Discharge:** On eighty-seventh day, burns healed, chest clear; to Physical Therapy.

Case 3.—Male, age 23. The patient was in the room in which the fire started, was unable to go upstairs because of the crowd so he covered his face with his handkerchief and sat on the stairs until a fireman led him out of the building.

Condition on Arrival: He was conscious, in no shock, and with no respiratory difficulty. **Extent of Burn:** Slight first degree of nose and lips, slight inhalation.

Plasma Therapy: None. **Blood Pressure:** Normal. **Clinical Course:** He was discharged to the Army Base the morning after the fire. **Pulmonary Complication:** Patient had a few râles in the right chest but no difficulty in breathing. **Subsequent Transfusions:** None.

Chemotherapy: None. **Operations:** None. **Discharge:** First day, condition good.

Case 4.—Female, age 27. In the scramble the patient was knocked down, trampled upon and recalls inhaling smoke before she lost consciousness. She had not covered her face.

Condition on Arrival: She was conscious, in moderate shock, and coughing with râles at the left base.

Extent of Burn: Second degree: face. Total 2%. Corneal and inhalation burns present.

Plasma Therapy: Three units in the first 24 hours. **Blood Pressure:** Remained essentially unchanged. **Laboratory Data:** Maximum hematocrit 50% at 63 hours. NPN on fourth day was 62 mg. All other determinations were normal.

Clinical Course: The burns of the skin healed without event. **Pulmonary Complication:** Patient continued to have moist, productive cough for several days. Lungs gradually cleared during the next two weeks by physical examination. **Subsequent Transfusions:** None.

Chemotherapy: Sulfadiazine until the fifth day. **Penicillin:** None. **Operations:** None. **Discharge:** On fourteenth day, burns healed, lungs clear.

Case 5.—Male, age 30. Patient was overcome by dense smoke and lost consciousness; regained it only after admission to the hospital.

Condition on Arrival: He was unconscious but in no shock. He had considerable difficulty in breathing and was cyanotic, with râles in both chests.

Extent of Burn: First degree: face, nares, lips. Second degree: Elbow. Total: 3.5%. Slight inhalation burn.

Plasma Therapy: None. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit was 55% at 37 hours, with a plasma protein of 8.7 gm. Blood remained concentrated for seven days. All other determinations were normal.

Clinical Course: Burns healed within two weeks. *Pulmonary Complication:* Patient continued to have respiratory difficulty, with symptoms similar to those of asthma. Relieved by adrenalin and steam inhalations. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine continued until fourteenth day. *Penicillin:* None. *Operations:* None.

Discharge: On fifteenth day, condition good. Follow-up on thirty-second day: No respiratory symptoms, normal examination of chest.

Case 6.—Female, age 16. Patient remembers inhaling hot smoke and being trampled upon in the confusion before she lost consciousness.

Condition on Arrival: She was unconscious, in mild shock, was hoarse, and had rapid respirations. *Extent of Burn:* Second degree: finger. Total: 0.5%. Inhalation burns.

Plasma Therapy: One unit in the first 24 hours. *Blood Pressure:* 80 systolic recorded at fifth hour, normal after plasma. *Laboratory Data:* Maximum hematocrit was 50% at 56 hours. Blood potassium on fifteenth day was 5.4 m.Eq. Arterial punctures on third and fifth days (see article on Shock). Metabolic observations recorded in article.

Clinical Course: Burn healed promptly. *Pulmonary Complication:* Increasing respiratory difficulty required oxygen therapy and aminophyllin during the first three days. Roentgenogram showed collapse of both lower lobes. Patient improved over the next three weeks, coughing up occasional plugs of mucus. On discharge the lungs were essentially normal. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine continued until twenty-fourth day. *Penicillin:* None. *Operations:* None.

Discharge: On twenty-fourth day, condition relieved.

Case 7.—Male, age 29. History could not be obtained.

Condition on Arrival: Patient was maniacal, uncontrollable, vomiting. Blood pressure 120/70. Evidence of smoke inhalation. Paraldehyde (4 cc. i.v.) given, successful in controlling hyperactivity.

Extent of Burn: Second and third degree: Face, hands, scalp. Total: 11%. Inhalation burn.

Plasma Therapy: Three and 2/5 units on first day. *Blood Pressure:* Continued normal. *Laboratory Data:* Highest hematocrit was 53% at 15 hours. Blood chlorides reached 118 m.Eq. at 37 hours. All other determinations, including blood potassium of 4.1 m.Eq. on first day, normal.

Clinical Course: Paraldehyde necessary to control patient. *Pulmonary Complication:* Tracheal râles developed. Aminophylline administered. Tracheotomy performed 24 hours after admission. Roentgenogram of the chest on the second day showed atelectasis. Put in oxygen tent. Early morning of third day temperature rose to 107° F, with respirations gasping and labored but without any obstruction at tracheotomy. Pulse which had risen to 160 dropped to 90 and became weak and thready. Blood pressure still 100/70. Died shortly thereafter. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine throughout the first day. *Operation:* Tracheotomy 24 hours after admission.

Discharge: Died early on third day. Postmortem roentgenograms showed pulmonary edema and trapped air in the left lung. (Autopsy: See article by Mallory and Brickley.)

Case 8.—Female, age 29. History was not obtained.

Condition on Arrival: Conscious, moderate shock, cyanotic.

Extent of Burn: Second degree: Face, neck, arms, hands, back, legs. Third degree: Hands, arms, shoulders, forehead, back. Total: 29.1%. Inhalation burn. (See color section, Fig. 12.)

Plasma Therapy: Four units on first day, four units on second day. *Blood Pressure:* Down to 95/70. *Laboratory Data:* Highest hematocrit 65% at 11 hours, fell rapidly to 50% at 15 hours. Developed moderate anemia. Metabolic observations recorded in article. Had elevated NPN on seventeenth day (see article on Shock).

Clinical Course: Abnormal growth of hair on face, thick on cheeks; also noted on extremities. Catamenia absent. *Pulmonary Complication:* Developed marked hoarseness and rhonchi. Atelectasis by roentgenogram on fourth day, trapped air on third day. Chest signs persisted by roentgenogram for eleven days. Vital capacity 51% on tenth day. On twenty-eighth day patient developed signs of pulmonary infarct, confirmed by roentgenogram; leg veins ligated. *Subsequent Transfusions:* Four of whole blood.

Chemotherapy: Sulfadiazine for first 48 days. Penicillin from sixth through thirty-ninth days. *Operations:* Bilateral superficial femoral vein ligation, twenty-eighth day; no clots found. Split-thickness skin grafts to hands, arms and forehead on thirty-ninth day.

Discharge: On sixty-third day to Physical Therapy, healed.

Case 9.—Female, age 22. Patient was not burned but inhaled considerable smoke and fumes. When she reached the outside she began to vomit as she coughed, and became unconscious for a few minutes.

Condition on Arrival: Conscious, no shock, coughing.

Extent of Burns: None, except inhalation.

Plasma Therapy: None. *Blood Pressure:* Normal. *Laboratory Data:* Blood chloride 117 m.Eq. on second day. Other determinations normal.

Clinical Course: Pulmonary Complication: Patient developed cough and moderate expectoration of mucoid sputum; chest examination and roentgenogram negative. Discharged in two days. *Subsequent Transfusions:* None.

Chemotherapy: None. *Operations:* None. *Discharge:* On second day, condition improved.

Case 10.—Male, age 24. Patient sprained ankle getting out of fire.

Condition on Arrival: Patient was conscious, in no shock, had no respiratory difficulty.

Extent of Burns: First degree: Face. Total: 1%.

Plasma Therapy: None. *Blood Pressure:* Normal. *Laboratory Data:* Hematocrit 54% on second day. Other determinations normal.

Clinical Course: Roentgenogram of left ankle showed no evidence of fracture; ankle was strapped. Patient had no other clinical complaints. *Pulmonary Complication:* Roentgenogram of chest was normal. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine continued until second day. *Penicillin:* None. *Operations:* None. *Discharge:* On second day, condition good.

Case 11.—Male, age 24. Patient arrived at the Cocoanut Grove about 20 minutes before the fire started. Standing near the stairway, he saw flames coming up the stairs. He was pushed by the crowd away from the source of the fire. Eventually he fell to the floor. He remembers nothing after that until he arrived at the hospital.

Condition on Arrival: Shock impending.

Extent of Burns: Second degree: Face, neck, arms, hands, back, legs. Third degree: Arm, hand, back, shoulder, knee. Total: 29%. Inhalation burns.

Plasma Therapy: Nine units on first day. *Blood Pressure:* Normal at first and soon after reaching the ward the patient was taken off shock blocks. About three hours after admission, signs of shock set in, the blood pressure falling as low as 82/56. Shock treatment was reinstituted. Lab-

oratory Data: Highest hematocrit reading was 64% at 12 hours, dropping slowly to 56% at 45 hours, and 45% at 67 hours. Blood potassium and other determinations normal except for mild anemia. Metabolic observations recorded in article.

Clinical Course-Pulmonary Complication: Patient developed Cheyne-Stokes respiration and hoarseness, with bronchial breath sounds, no râles, mild cough. Chest remained clear by roentgenogram. Vital capacity was 78% on seventh day. *Subsequent Transfusions:* One of whole blood.

Chemotherapy: Sulfadiazine for first 28 days. Penicillin from sixth through twenty-eighth day. Sulfadiazine again from thirty-eighth through forty-fourth days. *Operations:* Skin graft to right hand and arm, left upper arm and right knee on thirty-eighth day. Ligation of right superficial femoral vein on forty-first day, no clot found. Ligation of left superficial femoral vein on sixty-ninth day, clot found. Skin graft to back on eighty-fourth day.

Discharge: On one hundred and third day, healed, to Physical Therapy.

Case 12.—Male, age 23. History not obtained.

Condition on Arrival: In marked shock, no cyanosis, but râles at the right base and burned nostrils. Denuded burned surfaces were cherry-red color; (exposed mucous membranes were covered with soot).

Extent of Burns: Second and third degree: Face, scalp, neck, ears, back, hands. Estimated total: 19%. Inhalation burns.

Plasma Therapy: Five units in first 24 hours. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit was 61% at six hours, dropping to 51% at 23 hours.

Clinical Course-Pulmonary Complication: Patient developed considerable edema of the neck and remained semiconscious and very restless during the first day. After 27 hours, chest roentgenogram having been negative at 12 hours, patient rapidly developed upper respiratory obstruction and, despite immediate emergency tracheotomy, died. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine on first day. Penicillin: None. *Operation:* Tracheotomy on second day. *Discharge:* On second day, dead.

Case 13.—Female, age 20. Patient was standing near the telephone booth when she saw flames spread over the ceiling. She tried to run to the main entrance, which was nearby, but was knocked down and trampled on by the crowd. The smoke was very thick and made her cough. The crowd kept her from getting out the main entrance so she tried to get out through another door which she knew existed near the orchestra stand, in the opposite direction. She was knocked down three more times and felt the flames hissing on her legs. She fell to the floor and thereafter remembered nothing more until her fifth day in the hospital.

Condition on Arrival: In profound shock, labored respirations, cyanotic, voice hoarse, pulse 150, temperature 94° F.

Extent of Burns: Second degree: Face, neck, scalp, back, arms, hands, legs. Third degree: Face, neck, scalp, back, arms, hands, legs. Total: 56%. Inhalation burn. (See colored photographs, Fig. 11).

Plasma Therapy: Seven units on first day, two units on second day. *Blood Pressure:* Burned areas prevented taking this during early days. *Laboratory Data:* Highest hematocrit 53% at 10 hours. Arterial puncture on fourth and fifth days (see article on Shock). Metabolic observations recorded in article.

Clinical Course: Both saphenous veins were cannulated at the ankles and fluid run in rapidly. Showed marked restlessness. General condition rapidly improved. The wound of a sternal transfusion became infected. The patient developed psychiatric disturbances. After the major areas of burn had been grafted, patient's general condition improved further and her psychiatric disturbance entirely cleared up. Abnormal heavy

growth of hair occurred on all extremities. Catamenia absent. *Pulmonary Complication:* Lungs were clear by roentgenogram on the first day, evidence of trapped air appeared on the second day. Course thereafter was stormy. Atelectasis and trapped air were still visible in the lungs after 119 days. *Subsequent Transfusions:* Twenty-five whole blood transfusions.

Chemotherapy: Sulfadiazine given for first 28 days. Penicillin: From sixth through forty-first day. Sulfadiazine again given from thirty-fourth through one hundred and fortieth day. *Operations:* Incision and drainage of chest abscess on twelfth day. Amputation of fingers, rt. hand, on thirty-third day. Skin grafts to legs on seventy-fourth day. Skin grafts to right hand, forehead, scalp and chest wall on eighty-eighth day. Skin graft to right leg on one hundred and tenth day. Skin grafts to legs and scalp on one hundred and twenty-fourth day.

Discharge: One hundred and forty-third day. Only small unhealed areas remain.

Case 14.—Male, age 29. Patient saw a sheet of flame burst out near the bar. Heavy smoke appeared after the lights went out. Patient breathed through his hands and only got a few whiffs of fumes. He got near the door and was pulled out by somebody, he thinks three or four minutes after the first flash.

Condition on Arrival: Fair, conscious, no immediate shock, râles at lung bases.

Extent of Burns: Second degree: Face, hands. Total: 7%. Inhalation burns.

Plasma Therapy: Four units on first day. *Blood Pressure:* 130/80 four hours after admission. *Laboratory Data:* Maximum hematocrit was 57% at 17 hours. All other determinations were normal.

Clinical Course: Condition remained good, burns remained clean. *Pulmonary Complication:* Vital capacity 83% on seventh day. Lungs cleared rapidly. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine until discharge. *Operations:* Ligation of left long saphenous vein on ninth day, no clot found.

Discharge: On twelfth day to Fort Banks Hospital, with burns incompletely healed.

Case 15.—Male, age 30. Patient was seated at a table in the Melody Lounge, heard cry of "fire" and walked across stage. Lights went out, smoke became heavy. Patient lost consciousness, woke up in the street being given artificial respiration.

Condition on Arrival: Conscious and responsive, no shock, respirations regular and easy.

Extent of Burns: First degree: face. Second degree: Neck. Total: 4%. Slight inhalation burns.

Plasma Therapy: None. *Blood Pressure:* Remained normal. *Laboratory Data:* Hematocrit highest at 52% at 37 hours. All other determinations normal.

Clinical Course: Burns remained clean. *Pulmonary Complication:* Minor chest signs developed. Vital capacity 102% on seventh day.

Chemotherapy: Sulfadiazine until discharge. *Operations:* None.

Discharge: On tenth day, healed. Returned on thirty-fourth day to Psychiatric Service; committed suicide eight days later (see article by Cobb and Lindemann).

Case 16.—Male, age 58. Patient was knocked down, trampled on, and inhaled a considerable amount of thick, black oily smoke. He was pulled out of the building within a few minutes of the start of the fire.

Condition on Arrival: Conscious, not in shock, coughing considerably but color good.

Extent of Burns: Second degree: Face, neck, hands. Total: 5.5%. Slight inhalation burn.

Plasma Therapy: One unit in first 24 hours. *Blood Pressure:* Remained normal throughout. *Laboratory Data:* Maximum hematocrit 54% at 37 hours. Blood chloride 115 mEq. on fourth day. All other determinations normal.

Clinical Course: Burns healed uneventfully. *Pulmonary Complication:* Respiratory difficulty rapidly cleared. *Subsequent Transfusions:* None. *Chemotherapy:* Sulfadiazine continued until twelfth day. Penicillin from sixth to eighth days. *Operations:* None. *Discharge:* On twelfth day, burns of left hand clean but not healed; healed by six weeks.

Case 17.—Female, age 43. In the confusion of the fire patient was knocked to the floor and was trampled by several people. She held her breath in order to avoid inhaling fumes, and was quickly led from the building by a fireman.

Condition on Arrival: Conscious, no shock, normal breathing.

Extent of Burns: Second degree: Face, hand, arm, shoulder. Total: 9%. Inhalation burns. (Face and hand debrided, cleansed and 5 per cent sulfathiazole ointment applied).

Plasma Therapy: One unit on second day. *Blood Pressure:* Remained normal throughout. *Laboratory Data:* Maximum hematocrit was 52% at 37 hours. Sulfadiazine level of bleb fluid was 2.2 mg. on seventh day; simultaneous blood level was 4.6 mg. Earlier sulfadiazine levels ranged from 9.1 mg. at sixth hour to 4.0 mg. at thirty-seventh hour.

Clinical Course—Pulmonary Complication: No respiratory symptoms but for the first two days had a few rales. Lungs entirely clear on discharge. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine continued until twelfth day. Penicillin: None. *Operations:* None.

Discharge: On twelfth day, burns of arm clean but not healed; healed at two weeks.

Case 18.—Female, age 42. Patient was in the balcony and tried to run from the flames when she lost consciousness. On coming to she was beneath a pile of bodies, and was pulled out by her legs.

Condition on Arrival: Conscious, no shock, no respiratory difficulty.

Extent of Burns: First and second degree: Face and hand. Total: 3.5%. Slight inhalation burns.

Plasma Therapy: One unit in first 24 hours. *Blood Pressure:* Normal throughout. *Laboratory Data:* Maximum hematocrit was 46% at 8 hours.

Clinical Course: Burned areas remained clean. *Pulmonary Complication:* Patient developed slight productive cough which gradually decreased. Chest examination was normal on discharge. *Subsequent Transfusions:* None.

Chemotherapy: None. *Operations:* None.

Discharge: On sixth day, burns clean, healed.

Case 19.—Male, age 42. Patient was in the main balcony, saw a flash of flames and thick smoke. He made his way downstairs with his fingers to his nostrils, and was pushed ahead by the throng. He remembers only taking one or two full breaths. Thereafter he recalls nothing.

Condition on Arrival: Conscious, evidence of smoke inhalation.

Extent of Burns: Second degree: Face, hands, scalp. Total: 5.5%. Severe inhalation burns.

Plasma Therapy: Four units in first day. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit 59% at 37 hours. Blood sulfadiazine level ranged from 5.5 mg. down to zero on seventh day on which day b.leb fluid level was 1.0 mg.

Clinical Course: The burns were a minor problem. *Pulmonary Complication:* Developed wheezing and other chest sounds a few hours after admission. Developed into severe bronchial asthma. Roentgenograms showed lobar emphysema with small areas of atelectasis on first day. Treated with adrenalin and aminophylline. Gradually improved. Chest roentgenogram still showed evidence of some trapped air in the eighteenth week. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine for first eight days. Penicillin sixth through twelfth days. *Operations:* Attempted tracheotomy on fourth day, not accomplished because of massive edema of neck.

Discharge: On thirty-second day, healed.

Case 20.—Female, age 38. Patient's history was not obtained.

Condition on Arrival: Shock impending, cyanotic.

Extent of Burns: Second degree: Face, neck, back, scalp, arms, hands. Third degree: Arms, hands, shoulders. Total: 26.6% (see color section Fig. 10). Inhalation burn.

Plasma Therapy: Three units on first day.

Blood Pressure: Above 100 systolic throughout. *Laboratory Data:* Maximum hematocrit 55% at 6 hours. Blood potassium 3.3 and 3.7 m.Eq. on first day. Bleb fluid sulfadiazine 10.0 mg., with blood level of 10.6 mg. on seventh day. Metabolic observations recorded in article.

Clinical Course: General condition satisfactory. Required nasal-gastric feedings because of burns of pharynx. Abnormal growth of hair occurred on the lips, chin, and extremities. Absent cataplexia. *Pulmonary Complication:* Respirations labored with productive cough. Respiratory embarrassment increased, with tracheal rattle. Laryngoscopy showed edema of cords. On constant oxygen therapy. Tracheotomy performed. Patient became comatose but rallied gradually. Chest roentgenogram: See article by Schatzki. *Subsequent Transfusions:* Five of whole blood.

Chemotherapy: Sulfadiazine for first 24 days, leading to agranulocytosis (see article by Lyons). Penicillin from sixth through fortieth days. *Operations:* Tracheotomy on third day. Split-thickness skin grafts to arms and hands on thirty-ninth day. Split-thickness skin grafts to upper arms on sixty-seventh day.

Discharge: On eighty-fourth day, healed except for proximal interphalangeal joint of left index finger; tracheotomy wound healed.

Case 21.—Female, age 26. The patient was not burned but inhaled a considerable amount of smoke for 25 minutes. On reaching the street she expectorated a great deal of "black stuff."

Condition on Arrival: Conscious, in no shock, coughing.

Extent of Burn: None.

Plasma Therapy: None. *Blood Pressure:* Normal. *Laboratory Data:* None.

Clinical Course—Pulmonary Complication: Respiratory symptoms disappeared in 18 hours.

Chemotherapy: None. *Operations:* None.

Discharge: On first day, condition good.

Case 22.—Male, age 39. Patient's history was not obtained.

Condition on Arrival: In moderate shock, considerable difficulty in respiration. Cherry-red color of denuded burned surfaces. Mucous membranes were charred and sooty.

Extent of Burns: Second degree: Face, scalp, neck, hands. Total: 11%. Severe inhalation burns.

Plasma Therapy: Five units in 24 hours. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit 56% at 3 hours, 52% at 5 hours.

Clinical Course—Pulmonary Complication: For marked upper respiratory obstruction, tracheotomy had to be performed, at about 6 hours. Respiratory distress apparently more marked in expiration; continued despite adrenalin, aminophylline and oxygen therapy. Patient slowly failed and died 24 hours after original burn. *Subsequent Transfusion:* None.

Chemotherapy: Sulfadiazine continued until death. Penicillin: None. *Operation:* Tracheotomy on first day.

Discharge: On first day, dead.

Case 23.—Female, age 30. Patient was seated in Melody Lounge when fire started. She ran upstairs and across dance floor; fell and remained prostrate near an exit. The smoke was hot but she did not inhale much; did not cover her face. She did not lose consciousness. She was wearing a heavy coat with a fur collar. She was dragged to safety.

Condition on Arrival: Shock impending, no respiratory difficulty.

Extent of Burns: Second degree: Face, neck,

hands, knec. Third degree: neck, hands. Total: 11%. Slight inhalation burns.

Plasma Therapy: Four units on first day. *Blood Pressure:* Did not go below 105/60. *Laboratory Data:* Maximum hematocrit 61% at 17 hours. Secondary anemia with hematocrit of 24% and plasma protein of 5.5 Gm. on thirty-ninth day.

Clinical Course: Transitory mental confusion with restlessness. Abnormal growth of hair occurred on face, forearms and legs. There has been a patchy loss of this hair since return of catamenia. *Pulmonary Complication:* Minimal chest signs, chest roentgenograms remained negative. Vital capacity was 75% on seventh day. *Subsequent Transfusions:* Three of whole blood.

Chemotherapy: Sulfadiazine for first 12 days; developed drug fever. Penicillin sixth through fourteenth days, and again twenty-first through twenty-ninth days. *Operations:* Skin graft to both hands on thirty-seventh day; complete loss of both grafts. Skin graft to both hands and wrist on fifty-second day; partial take. Skin graft to right hand on sixty-ninth day.

Discharge: On eighty-third day, healed, to Physical Therapy.

Case 24.—Male, age 29. Patient remembers no details.

Condition on Arrival: Conscious, in no shock, slightly cyanotic.

Extent of Burns: First and second degree: Face, neck, nostrils, tongue. Total: 2%.

Plasma Therapy: None. *Blood Pressure:* Remained normal. *Laboratory Data:* None.

Clinical Course: Patient discharged approximately 20 hours following the fire with no complaints except difficulty in swallowing.

Chemotherapy: None. *Operations:* None.

Discharge: On first day to Fort Banks Hospital, condition apparently good.

Case 25.—Male, age 46. No history obtained. *Condition on Arrival:* Extremely hyperactive. Respiratory embarrassment required intermittent oxygen. Shock impending. Cherry-red color of denuded burned surfaces, mucous membranes charred and sooty.

Extent of Burns: Second and third degree: Face, scalp, hands, arms, back. Estimated total: 8%. Severe inhalation burns. Corneal burns.

Plasma Therapy: Five units on first day, one on second. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit 57% at 3 hours, dropped to 48% at 17 hours. Terminal rise in NPN to 64 mg., terminal blood potassium 4.2 m.Eq.

Clinical Course.—*Pulmonary Complication:* Restlessness became extreme. Respiratory embarrassment increased, required constant oxygen therapy. Marked hoarseness, unable to swallow. Roentgenogram. See article by Schatzki. Paradoxical pulse developed.

Chemotherapy: Sulfadiazine for two days. *Operations:* None.

Discharge: On second day, dead. (Autopsy: See article by Mallory and Brickley.)

Case 26.—Male, age 36. Patient was sitting at a table directly in front of the stage. On seeing the fire he headed toward the kitchen in the rear. He went down a short flight of stairs and found himself outdoors. He then reentered to search for the rest of his party, and following this remembered nothing until his arrival at the hospital. Patient covered his face with a water-soaked napkin and tried to keep close to the floor.

Condition on Arrival: Fair, with shock impending. No respiratory embarrassment. Shivering.

Extent of Burns: Second degree: Face, hands. Total 2.5%. Inhalation burns. Corneal burns.

Plasma Therapy: One unit on first day. *Blood Pressure:* 80 systolic on arrival, rose in one-half hour to normal and remained so. *Laboratory Data:* Maximum hematocrit 52% at 17 hours. Blood potassium 4.3 m.Eq. on both first and second days. All other determinations also normal.

Clinical Course: General condition remained

good. *Pulmonary Complication:* Lungs remained clear until second day when some râles developed. Roentgenograms of the chest on the first and second days were negative. On the third day some atelectasis and trapped air were seen, and were still present on the eighteenth day. Vital capacity 56% on tenth day. *Subsequent Transfusion:* None.

Chemotherapy: Sulfadiazine for first 12 days. Drug fever and rash developed. *Operations:* None.

Discharge: On twenty-first day, chest clear and burns completely healed.

Case 27.—Female, age 18. History was not obtained.

Condition on Arrival: Manic and hysterical, in moderate shock, considerable difficulty with respiration.

Extent of Burns: Second and third degree: Face, arms, back, buttocks, hands. Total: 22%. Inhalation burn.

Plasma Therapy: Eight units in first 24 hours, five units second and third days. *Blood Pressure:* Dropped to 80/60 soon after admission, gradually rose. *Laboratory Data:* Maximum hematocrit was 56% at 3 and 11 hours (see Fig. 47, article on Shock).

Clinical Course: Acute dilatation of the stomach was relieved by aspiration with a catheter. Adrenal cortical extract was given. *Pulmonary Complication:* Continued to have respiratory difficulty, requiring artificial respiration and oxygen administration. Aminophylline was given for the bronchiolar obstruction without effect. Developed paradoxical pulse. She rapidly failed and on the third day died of pulmonary failure. *Subsequent Transfusion:* None.

Chemotherapy: Sulfadiazine continued until death. *Operation:* None.

Discharge: On third day, dead. (Autopsy: See article by Mallory and Brickley.)

Case 28.—Female, age 26. Patient was sitting in Melody Lounge; saw the palm tree catch on fire. When the fire spread across the ceiling she tried to run up the stairs but the flames burned her back. She breathed in a lot of smoke and fumes, fell and became unconscious.

Condition on Arrival: Shock impending. Had minimal hoarseness.

Extent of Burns: Second degree: Face, neck, back, hands, arms. Third degree: Back, hand, arm. Total: 24.5%. Corneal burn. Inhalation burn (see color section, Fig. 16).

Plasma Therapy: Eight units on first day, two on second day, one on third day. *Blood Pressure:* Dropped to 80/55 on first morning, prompt return to normal. *Laboratory Data:* Maximum hematocrit was 64% at 11 hours. Blood potassium was 3.7 m.Eq. on second day. Bleb fluid sulfadiazine was 6.7 mg. and blood level 6.6 mg. on fifth day; on the sixth day bleb fluid level 6.0 mg., and seventh day blood level 4.0 mg.; on the twelfth day bleb fluid 4.9 mg., with blood levels of 4.1 mg. on tenth day and only smallest possible trace on fourteenth day.

Clinical Course: Abnormal growth of hair occurred on arms and legs, slight on face. Absent catamenia. *Pulmonary Complication:* Breath sounds somewhat diminished on left. Roentgenogram negative. *Subsequent Transfusion:* One whole blood on sixteenth day.

Chemotherapy: Sulfadiazine for first 12 days. Drug fever and rash developed. Penicillin given from sixth through twenty-eighth days. *Operations:* Skin graft to hand and arm on fifty-first day.

Discharge: On sixty-seventh day, completely healed except for small spot on back; subsequently healed. To Physical Therapy.

Case 29.—Male, age 40. Patient was in the new bar when the fire started. When on his way to the door saw a sheet of flame and smoke. He was pulled out by a fireman, fainted, and recovered consciousness on arrival at the hospital.

Condition on Arrival: Shock impending, few râles in the chest.

Extent of Burns: Second degree: Face, ears, scalp, hands, arms. Third degree: Hands, arms, scalp. Total 12.5%. Inhalation burn (see color section, Fig. 15).

Plasma Therapy: Six units on first, and one on second days. *Blood Pressure:* Normal. *Laboratory Data:* Maximum hematocrit 61% at 10 hours; otherwise all determinations were normal.

Clinical Course-Pulmonary Complication: Small areas of atelectasis developed in the right chest as shown by roentgenogram from fourth to eleventh days. Vital capacity 79% on seventh day, 135% on tenth day. *Subsequent Transfusion:* None.

Chemotherapy: Sulfadiazine for first 28 days. Penicillin from twenty-second through twenty-eighth days. *Operations:* Skin graft to left hand on twenty-third day. Skin graft to right hand on thirty-fifth day.

Discharge: On fortieth day, healed, to Physical Therapy.

Case 30.—Female, age 24. Patient was in the main room opposite the stage; saw people running from the main entrance followed by thick clouds of smoke. She saw no flame. She escaped through the kitchen. The smoke was very bad. After having fallen to the floor she was dragged by her husband through a window. She lost consciousness partially.

Condition on Arrival: Good, some evidence of smoke inhalation.

Extent of Burns: No surface burns. Slight inhalation burns.

Plasma Therapy: None. *Blood Pressure:* Normal. *Laboratory Data:* Hematocrits normal. Blood chloride level was slightly elevated for four days; otherwise all determinations were normal.

Clinical Course: Had nausea and vomiting, headache. *Pulmonary Complication:* Developed moist râles in chest. Chest remained clear by roentgenogram.

Chemotherapy: Sulfadiazine on first day only. *Operation:* None.

Discharge: On sixth day, condition good.

Case 31.—Male, age 27. Patient was exposed to smoke for about 25 minutes while dragging his wife and other people out of the fire. He became unconscious and was carried across the street where he regained consciousness in a few minutes; took a taxi to the hospital.

Condition on Arrival: Good, calm, no respiratory difficulty, covered with soot.

Extent of Burns: Second degree: Lips, nares. Total: 0.5%.

Plasma Therapy: None. *Blood Pressure:* Normal. *Laboratory Data:* None.

Clinical Course: General condition remained excellent. *Pulmonary Complication:* Developed some coarse rhonchi, râles in the chest, and coughed up smoky mucus.

Chemotherapy: None. *Operation:* None.

Discharge: On first day to Fort Banks Hospital.

Case 32.—Female, age 35. History not obtained. *Condition on Arrival:* Profound shock, unconscious, with stertorous breathing. Cherry-red color of burns and mucous membranes.

Extent of Burns: Second degree: Face, hand, forearm. Total: 6%. Severe inhalation burns.

Plasma Therapy: Six units on first day, two on second, and three on third. *Blood Pressure:* Returned to normal after first three units of plasma. *Laboratory Data:* Hematocrit was never above normal but varied between 29 and 40% for first four days; arterial blood oxygen content 10.0 vol. % on third day; whole blood transfusions were given. Plasma protein was never below 6.9 gm. Blood potassium was 3.2 m.Eq. on first day. Prothrombin time was prolonged on fourth day. Blood chloride was 121 m.Eq. on second day. Van den Bergh was 7.3 mg. on seventh day.

Clinical Course: The burns were a minor problem. Was extremely restless, given paraldehyde.

Pulse not obtainable. Remained unresponsive and often had a senseless grin on her face. Psychiatric consultant felt that there was severe cerebral damage which was irreparable. *Pulmonary Complication:* Oxygen given immediately. Cyanosis increased and tracheotomy was performed. Roentgenogram showed areas of atelectasis from first to seventeenth days. *Subsequent Transfusions:* Two whole blood on third day; four whole blood later.

Chemotherapy: Sulfadiazine for first 13 days. Penicillin sixth through twelfth days. *Operation:* Tracheotomy on second day.

Discharge: On sixty-seventh day, burns healed, tracheotomy wound healed, lungs clear, evidence of central nervous system damage present.

Case 33.—Male, age 43. History not obtained. *Condition on Arrival:* Very poor; required oxygen.

Extent of Burns: Second and third degree: Face, hands, chest, back, abdomen, legs. Estimated total: 50%. Severe inhalation burns.

Plasma Therapy: Four units in first 12 hours. *Blood Pressure:* Normal. *Laboratory Data:* Hematocrit was 58% at 3 hours.

Clinical Course-Pulmonary Complication: Respiration and color remained poor. Coarse moist râles were present throughout lungs. Given coramine and aminophylline without avail.

Chemotherapy: Sulfadiazine once. *Operation:* None.

Discharge: 13 hours after injury, dead.

Case 34.—Female, age 40. History not obtained.

Condition on Arrival: Profound shock, unconscious, respiratory difficulty requiring oxygen.

Extent of Burns: Third degree: Face, neck, hands, back, legs, abdomen. Estimated total: 70%. Severe inhalation burns.

Plasma Therapy: Eight units in first day. *Blood Pressure:* Not obtainable. *Laboratory Data:* For determinations see Figure 46 in article on Shock.

Clinical Course: Color remained poor. Given adrenal cortical extract repeatedly. Roentgenogram first morning showed some atelectasis and acute dilatation of the stomach. Gastric aspiration carried out. Small urinary output. Condition remained poor.

Chemotherapy: Sulfadiazine first day. *Operation:* None.

Discharge: 26 hours after admission, dead.

Case 35.—Female, age 45. Patient was seated 30 or 40 feet from the head of the stairs when she saw a flash of flame coming up the stairs. She ran in the opposite direction, covering her face with her hat. She remembers that the room was filled with choking smoke and then she lost consciousness.

Condition on Arrival: Unconscious, in mild shock, breathing normally.

Extent of Burns: Second degree: Face, hand. Total: 3%. Corneal burns.

Plasma Therapy: One unit in first 24 hours. *Blood Pressure:* 74/55 on entry, rose to 90/60 in 8 hours and was thereafter normal. *Laboratory Data:* Maximum hematocrit was 43% at 17 hours. Blood chloride was 116 m.Eq. at 37 hours. Other determinations were normal.

Clinical Course: Because of the death of her husband in the fire the patient developed marked mental disturbance. Although further hospitalization and psychiatric care were advised, patient left the hospital against advice. *Pulmonary Complication:* Mild respiratory difficulty cleared within a week.

Chemotherapy: Sulfadiazine continued until ninth day. *Operation:* None.

Discharge: On tenth day, burns healed, with reactive depression.

Case 36.—Male, age 28. Patient stayed on the floor. Heat and smoke troubled him most. He was rescued by firemen. He retained consciousness throughout.

Condition on Arrival: Conscious, breath sounds were diminished at the right base, cyanotic.

Extent of Burns: Second degree: Face, scalp, neck, ears, hands. Third degree: Hands. Total: 8.5%. Corneal and inhalation burns.

Plasma Therapy: Five units on first day, two on second. *Blood Pressure:* Normal. *Laboratory Data:* Maximum hematocrit was 59% at 12 hours. Metabolic observations are given in article.

Clinical Course.—Pulmonary Complication: Marked hoarseness with diminution of breath sounds. Small areas of atelectasis by roentgenogram from fourth to eleventh days. Vital capacity 79% on tenth day. *Subsequent Transfusions:* One whole blood.

Chemotherapy: Sulfadiazine for first 12 days. Penicillin sixth through thirtieth days. *Operations:* Skin graft to both hands on twenty-fourth and thirty-fifth days. Left superficial femoral vein ligation on forty-seventh day, loose clot evacuated.

Discharge: On fifty-eighth day, burns healed, to Physical Therapy.

Case 37.—Male, age 52. Patient saw the room on fire suddenly, reached for a coat from the wall and covered his face. While struggling in the crowd he lost consciousness.

Condition on Arrival: Unconscious, cold, trembling, breathing deeply and steadily, not in shock.

Extent of Burns: Second degree: Face, neck, hand. Total: 3%. Corneal and inhalation burns.

Plasma Therapy: Three units in first 24 hours, one on second day. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit was 56% at 37 hours. Blood potassium was 3.5 mEq. on first day. All other determinations were normal. Metabolic observations recorded in article.

Clinical Course: Because of feeling of depression and anxiety over the death of his wife he had to be transferred to psychiatric service for two days before discharge. *Pulmonary Complication:* Within few hours developed cyanosis, cough, and showed râles in both lungs. Respiratory difficulty cleared during the next week. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine continued until fifteenth day. *Operation:* None.

Discharge: On seventeenth day, burns healed, lungs normal.

Case 38.—Male, age 36. Patient was at the main bar, saw smoke and flame coming up from downstairs. He was caught in a mob and carried in the direction of the new cocktail room; the smoke was severe. He was led downstairs by the crowd and into a small room from which there

was no exit. He lay down for 15 to 30 minutes. When no fire reached him he got up and climbed over bodies lying about. He heard somebody shout, "Here's a man who is still alive." He was put in a taxi and brought to the hospital. He never lost consciousness.

Condition on Arrival: Shock impending, no respiratory difficulty.

Extent of Burns: Second degree: Face, neck, scalp, back, hand, leg, foot. Third degree: Ankle. Total: 21.5%. Inhalation burns.

Plasma Therapy: Six units on first day, one on second, one on third. *Blood Pressure:* Remained normal. *Laboratory Data:* Maximum hematocrit was 63% at 6 hours. Blood potassium was 4.1 mEq. and 4.5 mEq. on first day, 4.5 mEq. on second day. Bleb fluid sulfadiazine level was 7.4 mg. on seventh day with simultaneous blood level of 6.4 mg. Blood level had been 9.5 mg. on fourth day. Had elevated NPN (see article on Shock).

Clinical Course: Nausea and vomiting for six days. *Pulmonary Complication:* No pulmonary symptoms or signs. Roentgenogram negative on second day. Small areas of atelectasis and small amount of trapped air by roentgenogram from fourth to eleventh days. Vital capacity 62% on seventh day. *Subsequent Transfusions:* None.

Chemotherapy: Sulfadiazine for first 11 days. Penicillin from fifth through eleventh days. *Operations:* None.

Discharge: On fourteenth day to Chelsea Naval Hospital, chest clear, burns unhealed.

Case 39.—Female, age 31. Patient was sitting in the gallery, fire appeared on opposite side. The lights went out, air was full of thick smoke. Patient fell with people on top of her. She struggled downstairs, semiconscious, water sprayed on her. Somebody carried her out.

Condition on Arrival: Profound shock, respiratory embarrassment, with scattered rhonchi.

Extent of Burns: Second degree: Face, hands. Total: 4%.

Plasma Therapy: Two units on first day. *Blood Pressure:* Systolic 90-99 for short period, otherwise normal. *Laboratory Data:* Maximum hematocrit 40% on first day. Elevated blood chloride, 120 mEq., at 37 hours. All other determinations normal.

Clinical Course: Improved rapidly. *Pulmonary Complication:* Minor chest signs. Roentgenogram showed evidence of some trapped air from third to tenth days. *Subsequent Transfusion:* None.

Chemotherapy: Sulfadiazine for first nine days. *Operations:* None.

Discharge: On tenth day, burns healed, chest clear.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D.
1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY
East Washington Square, Philadelphia, Pa.

INDEX TO VOLUME 117

A

- ABBOTT, W. E.: Fluid, Protein and Electrolyte Alterations in Experimental Intestinal Obstruction, 39.
- Abdominal Surgery, Preoperative Scrubbing in, 535; Preoperative Scrubbing in, 766.
- Abdomino-perineal Resection, Late Invasion of Bladder and Prostate in Cancer of the Rectum or Rectosigmoid, Following, 456.
- ABELS, JULES C.: Treatment of Postoperative Hypoproteincemia in Patients with Cancer of the Colon and Rectum, 748.
- Abortion or Miscarriage, Minimal Criteria Required to Prove Prima Facie Case of Traumatic, 596.
- Accessory Spleen in the Scrotum, 754.
- ACKERMANN, WOLFGANG: Diverticula and Variations of the Duodenum, 403.
- Acute Appendicitis During the Later Decades of Life: Some Remarks on the Incidence of the Disease in a Rural Area, 221.
- Acute Ileus, 427.
- Administration of Morphine and Antispasmodics in Biliary Colic, 207.
- Airway, Resuscitation and Sedation of Patients with Burns Which Include the, 825.
- ALDRICH, ROBERT HENRY: Forensic Aspects of Burns, 576.
- Alimentation in the Surgery of Peptic Ulcer, The Indications for Jejunal, 387.
- ALLEN, PHILIP D.: Umbilical Discharge in Acute Appendicitis, 473.
- Ampulla of Vater, Cyst of the, 728.
- Analgesia in Surgery, Continuous Caudal, 321.
- Aneurysm of the Brachial Artery, 791; of the Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, Traumatic Arteriosclerotic, 793.
- Announcement by American Urologic Society, 800.
- Antispasmodics and Morphine, Administration of, in Biliary Colic, 207.
- Appendicitis, Acute, during the Later Decades of Life: Some Remarks on the Incidence of the Disease in a Rural Area, 221; and other Visceral Lesions, Hyperesthesia of the Posterior Peritoneum (Objective Pain) in, 735; Umbilical Discharge in Acute, 473.
- ARIEL, IRVING: Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract. XII—The Glycerine Tolerance Test in Patients with Gastric Cancer, 740.
- Arteries, Restoration of Blood Flow, in Damaged, 481.

- Arteriosclerotic Aneurysm of the Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, Traumatic, 793.
- Artery, Aneurysm of the Brachial, 791; Tibial, Simulating an Osteogenic Sarcoma of the Fibula, Traumatic Arteriosclerotic Aneurysm, 793.
- Atresia of the Common Bile Duct, Congenital, 723; of the Duodenum, 718.
- ATWATER, JOHN S.: Gastrojejunal Colic Fistulae: With Special Reference to Associated Nutritional Deficiencies and Certain Surgical Aspects, 414.
- AUB, JOSEPH C.: The Pulmonary Complications: A Clinical Description, 834.

B

- BANKS, ROLAND W.: Islet Cell Carcinoma of Pancreas, with Metastasis, 437.
- BARCHAM, IRVING: A Study of Plasma Protein Variations in Surgical Patients, 52.
- BARR, J. HAROLD: The Administration of Morphine and Antispasmodics in Biliary Colic, 207.
- BEECHER, HENRY K.: Resuscitation and Sedation of Patients with Burns Which Include the Airway, 825.
- BENSON, CLIFFORD D.: Echinococcus Cyst of Lung Exhibiting Unusual Radiologic and Surgical Features, 268.
- BERMAN, J. K.: Empyema Complicated by Broncho-esophagopleural Fistula, 100; Preoperative Scrubbing in Abdominal Surgery, 535, 766.
- BEST, R. RUSSELL: The Administration of Morphine and Antispasmodics in Biliary Colic, 207.
- Bile Duct, Congenital Atresia of the Common, 723; Congenital Cystic Dilatation of the Common, 355.
- Biliary Colic, Administration of Morphine and Antispasmodics in, 207.
- Biliary Dyskinesia from the Surgical Viewpoint, 198.
- BILLINGS, F. T.: Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon the Peritoneum, 677; Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Memolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670.
- BINKLEY, GEORGE E.: The Treatment of Postoperative Hypoproteincemia in Patients with Cancer of the Colon and Rectum, 748.
- BISGARD, J. DEWEY: Substitution of the Urinary Bladder with a Segment of Sigmoid, 106.
- Bladder and Prostate in Cancer of the Rectum or Rectosigmoid Following Abdominoperineal Resection, Late Invasion of, 456; with a Seg-

- ment of Sigmoid, Substitution of the Urinary, 106; Spontaneous Rupture of the Urinary, 760.
- BLAKEMORE, ARTHUR H.: Restoration of Blood Flow in Damaged Arteries, 481.
- BLODGETT, JAMES B.: An Improved Towel Clip, 637.
- Blood Bank, A Note on the, 928.
- Blood Circulation in Pedicle Flaps, 692; Flow, Restoration of, in Damaged Arteries, 481.
- BOENHEIMER, MILTON: A Study of Plasma Protein Variations in Surgical Patients, 52.
- BOOK REVIEWS: Atlas of Ovarian Tumors, by Gemma Barzilai. Reviewed by Arthur Purdy Stout, 639; Blood Substitutes and Blood Transfusion. Reviewed by Walter Estell Lee, 158; Ophthalmology and Otolaryngology: Military Surgical Manuals II. Reviewed by George W. Wood, 640; Sulfanilamide and Related Compounds in General Practice. Reviewed by J. E. Rhoads, 319; Synopsis of Traumatic Injuries of the Face and Jaws. Reviewed by Henry Sage Dunning, 319; Textbook on Fractures. Reviewed by Walter Estell Lee, 320; Yearbook of Industrial and Orthopedic Surgery. Reviewed by Henry Saltonstall, 800.
- BOOKS RECEIVED, 480; 800.
- Brachial Artery, Aneurysm of the, 791.
- BRANSFIELD, JOHN W.: Cleft Palate, 1.
- BRICKLEY, WILLIAM J.: Pathology: With Special Reference to the Pulmonary Lesions, 865.
- Broncho-esophagopleural Fistula, Empyema Complicated by, 100.
- BROOKS, BARNEY: Cyst of the Ampulla of Vater, 728.
- BROWDER, JEFFERSON: The Surgical Treatment of the Congenital Malformations Implicating the Distal Spinal Cord, 118.
- BRUBAKER, ROBERT E.: The Intra-abdominal Use of the Mikulicz Pack, 256.
- BRUCKNER, JOHN P.: Aneurysm of the Brachial Artery, 791.
- BRUES, AUSTIN M.: The Pulmonary Complications: A Clinical Description, 834.
- BUCHHOLZ, RANSOM R.: The Blood Circulation in Pedicle Flaps, 692.
- Buffered Sulfanilamide, Local use in Primary Closure of Pilonidal Cyst, 191.
- Burned, Severely, Rehabilitation of the Procedures in, 903.
- Burn Shock Complicated by Pulmonary Damage, The Problem of, 915.
- Burns as Influenced by Rapid Tanning and by Transfusions, Early Mortality of, 327.
- Burns, Forensic Aspects of, 576.
- Burns, Pathology of, 234.
- Burns, Treatment of the Surface, 885.
- BUTT, HUGH R.: Gastrojejuno-colic Fistulae: With Special Reference to Associated Nutritional Deficiencies and Certain Surgical Aspects, 414.
- C
- Calcification, Intracranial, 300.
- Calorie Intake and Weight Loss in Postoperative Convalescence. Nitrogen Metabolism, 512.
- Cancer of Colon and Rectum, Treatment of Postoperative Hypoproteinemia in Patients with, 748; of Gastro-intestinal Tract, Metabolic Studies in Patients with. XII—The Glycerine Tolerance Test in Patients with Gastric Ulcer, 740; of Rectum or Rectosigmoid Following Abdomino-perineal Resection, Late Invasion of Bladder and Prostate, in, 456; Total Gastrectomy for, 183.
- CANNON, BRADFORD: Procedures in Rehabilitation of the Severely Burned, 903; Rate of Epithelial Regeneration, 85.
- CANNON, IDA M.: Social Service Activities, 809.
- CAPURRO, RAFAEL: Hyperesthesia of the Posterior Peritoneum (Objective Pain) in Appendicitis and other Visceral Lesions, 735.
- Carcinoma of Gum, 74; of Pancreas (Islet Cell), with Metastasis, 437.
- CASTEN, DANIEL: Study of Plasma Protein Variations in Surgical Patients, 52.
- Caudal Analgesia in Surgery, Continuous, 321.
- Cavity, The Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic Staphylococcus Aureus Infections of the Pleural, 670.
- Chemotherapy and Infection, Problems of, 894.
- Cholesterosis of the Gallbladder, 450.
- CHURCHILL, EDWARD D.: Lobectomy for Pulmonary Tuberculosis, 641.
- Circulation in Pedicle Flaps, Blood, 692.
- Cleft Palate, 1.
- Clip, An Improved Towel, 637.
- Clinical Uses of Vitallium, 772.
- COBB, STANLEY: Neuropsychiatric Observations, 814.
- Cochliomyia Americana Infestation in Man, 468.
- Cocoanut Grove Disaster, 801-965.
- Colic, Biliary, Administration of Morphine and Antispasmodics in, 207.
- Colon and Rectum, Treatment of Postoperative Hypoproteinemia in Patients with Cancer of the Colon and Rectum, 748.
- COLP, RALPH: Indications for Jejunal Alimentation in the Surgery of Peptic Ulcer, 387.
- Complications, Pulmonary: A Clinical Description, 834.
- Congenital Atresia of the Common Bile Duct, 723; Dilatation of the Common Bile Duct, 355; Hemangiomas of the Skin, Treatment of, 134; Malformations Implicating the Distal Spinal Cord, Surgical Treatment of, 118.
- Continuous Caudal Analgesia in Surgery, 321.
- COOPER, FREDERICK W., JR.: Atresia of the Duodenum, 718.
- COPE, OLIVER: Management of the Cocoanut Grove Burns at the Massachusetts General Hospital; Foreword, 801; Metabolic Observations, 937; The Problem of Burn Shock Complicated by Pulmonary Damage, 915; Rate of Epithelial Regeneration, 85; The Treatment of the Surface Burns, 885.
- Cord (Spinal), Surgical Treatment of the Congenital Malformations Implicating the Distal, 118.

- Co Tui: Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.
- Craniocerebral Injuries, Late Effects of, 544.
- CRAWFORD, ALBERT S.: Method of Prolonged Ventricular Drainage, 798.
- CRUTCHER, RICHARD R.: Effect of Sulfanilamide, Sulfathiazole and Sulfathiazine Upon the Peritoneum, 677; Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670.
- Cyst of Ampulla of Vater, 728; of Lung, Echinococcus, Exhibiting Unusual Radiologic and Surgical Features, 268; Pilonidal, Local Use of Buffered Sulfanilamide in Primary Closure, 191.
- Cystotomy, Transplantation of the Peritoneum During Suprapubic, 783.
- Cysts, Multilocular Serous, of the Round Ligament Simulating Incarcerated Herniae, 216.

D

- DANIEL, ROLLIN A., JR.: Carcinoma of the Gum, 74; Effect of Sulfanilamide, Sulfathiazole and Sulfathiazine Upon the Peritoneum, 677; Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670.
- DE AMESTI, FELIX: Total Gastrectomy for Cancer, 183.
- (De Quervain's Disease.) Stenosing Tendovaginitis at the Radial Styloid, 290.
- Diabetes, The Relation of Trauma to, 607.
- Dilatation of the Common Bile Duct, Congenital, 355.
- Discharge, Umbilical, In Acute Appendicitis, 473.
- Diverticula and Variations of the Duodenum, 403.
- DORRANCE, GEORGE M.: Cleft Palate, 1.
- DOUGLAS, BEVERLY: Blood Circulation in Pedicle Flaps, 692.
- Drainage, A Method of Prolonged, 798.
- Dressing, Application of, to the Severely Frozen Limbs of Dogs, Prevention of Shock and Death by Immediate Pressure, 686.
- DREYFUSS, M. L.: Accessory Spleen in the Scrotum, 754.
- DRUCKERMAN, LEONARD J.: The Indications for Jejunal Alimentation in the Surgery of Peptic Ulcer, 387.
- Duct, Congenital Atresia of the Common Bile, 723; Congenital Cystic Dilatation of the Common Bile, 355.
- DUNNING, HENRY SAGE: Review of Synopsis of Traumatic Injuries of the Face and Jaws, 319.
- Duodenal Obstruction in the Newborn, The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of, 348; Ulcer, Intractable, 498.
- Duodenum, Atresia of the, 718; Diverticula and Variations of the, 403.
- Dyskinesia, Biliary, from the Surgical Viewpoint, 198.

E

- Early Mortality of Burns as Influenced by Rapid Tanning and by Transfusions, 327.
- Echinococcus Cyst of Lung Exhibiting Unusual Radiologic and Surgical Features, 268.
- EDWARDS, WALDO B.: Continuous Caudal Analgesia in Surgery, 321.
- Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon the Peritoneum, 677.
- EGER, SHERMAN A.: Congenital Cystic Dilatation of the Common Bile Duct, 355.
- Electrolyte Alterations in Experimental Intestinal Obstruction, Fluid, Protein and, 39.
- ELMAN, ROBERT: Early Mortality of Burns as Influenced by Rapid Tanning and by Transfusions, 327.
- Emergencies, a Light, Compact Unit for the Intravenous or Intra-osseous Injection of Plasma in, 152.
- EMMETT, J. M.: Accessory Spleen in the Scrotum, 754.
- Empyema Complicated by Broncho-esophagopleural Fistula, 100.
- Epithelial, Rate of Regeneration of, 85.
- ERR, I. H.: The Pathology of Burns, 234.
- EVANS, EVERETT I.: The Mechanism of Shock in Intestinal Strangulation, 28.
- EVANS, WILLIAM A., JR.: Echinococcus Cyst of Lung Exhibiting Unusual Radiologic and Surgical Features, 268.
- Evolution of Spinal Fusion, 278.

F

- FARMER, A. W.: The Pathology of Burns, 234.
- FAXON, NATHANIEL W.: The problems of the Hospital Administration, 803.
- FELL, EGBERT H.: Prevention of Shock and Death by Immediate Application of a Pressure Dressing to the Severely Frozen Limbs of Dogs, 686.
- Fibula, Traumatic Arteriosclerotic Aneurysm of the Tibial Artery Simulating an Osteogenic Sarcoma of the, 793.
- First-stage Thoracoplasty, 315.
- Fistula, Empyema Complicated by Broncho-esophagopleural, 100.
- Fistulae, Gastrojejunoecolic, 414.
- Fluid, Protein and Electrolyte Alterations in Experimental Obstruction, 39.
- Forensic Aspects of Burns, 576.
- Foreword to Symposium on the Coconut Grove Disaster, 801.
- Fractures, Textbook on, Review, 320.
- FRY, WESLEY: Spontaneous Rupture of the Urinary Bladder, 760.
- Fusion, Spinal, Evolution of, 278.

G

- Gallbladder, Cholesterosis of the, 450.
- Gastrectomy for Cancer, Total, 183.
- Gastric Ulcer, Glycerine Tolerance Test in Patients with. Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract, 740.

I

- Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, The Pre- and Postoperative Use of a Metal-Tipped, 348.
- Gastro-intestinal Tract, Cancer of the, Metabolic Studies in Patients with. XII—The Glycerine Tolerance Test in Patients with Gastric Ulcer, 740.
- Gastrojejunoecolic Fistulae, 414.
- General Surgery, Trends in, 297.
- Glycerine Tolerance Test in Patients with Gastric Ulcer. Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract, 740.
- Goiter Incisions, 332.
- Gout, Tophaceous, the Surgical Treatment of, 161.
- GROSS, JOSEPH: Congenital Atresia of the Common Bile Duct, 723.
- GUBLER, JOHN A.: Transverse Megacolon Associated with Chronic Volvulus, 786.
- Gum, Carcinoma of the, 74.

H

- HANNO, HAROLD A.: Islet Cell Carcinoma of Pancreas, with Metastasis, 437.
- HANSELMAN, RUSSELL: Prevention and Death by Immediate Application of a Pressure Dressing to the Severely Frozen Limbs of Dogs, 686.
- HASEMAN, L.: Cochliomyia Americana Infestation in Man, 468.
- Head Injury, Mechanisms of, 562.
- Hemangiomas of the Skin, The Treatment of Congenital, 134.
- Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, The Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon, 670.
- Herniae, Incarcerated, Multilocular Cysts of the Round Ligament, Simulating, 216.
- HERTIG, ARTHUR TREMAIN: Minimal Criteria Required to Prove Prima Facie Case of Traumatic Abortion or Miscarriage, 596.
- HINGSON, ROBERT A.: Continuous Caudal Analgesia in Surgery, 321.
- HINTON, J. WILLIAM: The Intractable Duodenal Ulcer, 498.
- HIRSCH, SYDNEY: A New Two-way Valve, 313.
- HOLMAN, EMILE: First-stage Thoracoplasty, 315.
- Hospital Administration, The Problems of the, 803.
- HOUSER, ALAN D.: Preoperative Scrubbing in Abdominal Surgery, 535.
- HOWARTH, M. B.: Evolution of Spinal Fusion, 278.
- Hydrometrocolpos in Infancy, 635.
- Hyperesthesia of the Posterior Peritoneum (Objective Pain) in Appendicitis and Other Visceral Lesions, 735.
- Hyperthyroidism, Reduction of the Mortality in the Surgical Management of: The Use of the Short Interval Two-stage Lobectomy, 263.
- Hypoproteinemia in Patients with Cancer of the Colon and Rectum, Treatment of Postoperative, 748.

- Ileus, Acute, 427.
- Improved Tip for Miller-Abbott Tube, 159.
- Improved Towel Clip, An, 637.
- Incarcerated Herniae, Multilocular Cysts of the Round Ligament, Simulating, 216.
- Incisions, Goiter, 332.
- Indications for Jejunal Alimentation in the Surgery of Peptic Ulcer, 387.
- Infancy, Hydrometrocolpos in, 635.
- Infection and Chemotherapy, Problems of, 894.
- Infections of the Pleural Cavity, The Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic Staphylococcus Aureus, 670.
- Infestation in Man, Cochliomyia Americana, 468.
- Injury, Mechanisms of Head, 562.
- Intra-abdominal Use of the Mikulicz Pack, 256.
- Intracranial Calcification, 300.
- Intractable Duodenal Ulcer, 498.
- Intra-osseous Injection of Plasma in Emergencies, a Light, Compact Unit for, 152.
- Intrathoracic Neuroblastoma, 93.
- Intravenous or Intra-osseous Injection of Plasma in Emergencies, a Light, Compact Unit for, 152.
- Intrinsic Knee Joint Lesions, Surgical Treatment of, 140.
- Islet Cell Carcinoma of Pancreas, with Metastasis, 437.

J

- Jejunal Alimentation in the Surgery of Peptic Ulcer, Indications for, 387.
- JOHNSON, GEORGE S.: Carcinoma of the Gum, 74; Treatment of Congenital Hemangiomas of the Skin, 134.
- JOHNSON, ROBERT A.: Umbilical Discharge in Acute Appendicitis, 473.
- JONES, FLORENCE: Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract. XII—The Glycerine Tolerance Test in Patients with Gastric Cancer, 740.
- JONES, THOMAS E.: Intra-abdominal Use of the Mikulicz Pack, 256.
- JOSLIN, ELLIOTT P.: The Relation of Trauma to Diabetes, 607.

K

- KERNODLE, E. B.: Reduction of Mortality in the Surgical Management of Hyperthyroidism: The Use of the Short Interval Two-stage Lobectomy, 263.
- KERSHNER, DAVID: Multilocular Serous Cysts of the Round Ligament Simulating Incarcerated Herniae, 216.
- KIRSHBAUM, JACK D.: Traumatic Arteriosclerotic Aneurysm of the Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, 793.
- KLOPSTOCK, ROBERT: Lobectomy for Pulmonary Tuberculosis, 641.
- Knee Joint Lesions, The Surgical Treatment of Intrinsic, 140.

- KRAFT, GEORGE: Traumatic Arteriosclerotic Aneurysm of the Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, 793.
KURTZ, WILLIAM A.: Preoperative Scrubbing in Abdominal Surgery, 535.
KYMAN SEYMOUR: Congenital Atresia of the Common Bile Duct, 723.

L

- LAHEY, FRANK H.: Goiter Incisions, 332.
Late Invasion of Bladder and Prostate in Cancer of the Rectum or Rectosigmoid Following Abdomino-perineal Resection, 456.
Law and Surgery, Symposium on Problems Relating to, 544.
LEE, WALTER E.: Intrathoracic Neuroblastoma, 93.
LEE, WALTER ESTELL: The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, 348; Review of Blood Substitutes and Blood Transfusions, 158; Review of Textbook on Fractures, 320.
Lesions, Hypcresthesia of the Posterior Peritoneum (Objective Pain) in Appendicitis and other Visceral, 735; Pulmonary, with Special Reference to the: Pathology, 865; Roentgenologic Report of the Pulmonary, 841.
LEWIS, KENNETH M.: Cholesterosis of the Gallbladder, 450.
LIGHT, RUDOLPH A.: Intracranial Calcification, 300; Treatment of Congenital Hemangiomas of the Skin, 134.
LINDEMANN, ERICH: Neuropsychiatric Observations, 814.
LINTON, ROBERT R.: The Surgical Treatment of Tophaceous Gout, 161.
Lipoma, So-called Retroperitoneal, 110.
Lobectomy for Pulmonary Tuberculosis, 641.
Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670; Use of Buffered Sulfanilamide in Primary Closure of Pilonidal Cyst, 191.
LORD, JERE W.: Restoration of Blood Flow in Damaged Arteries, 481.
Lung, Echinococcus Cyst of, Exhibiting Unusual Radiologic and Surgical Features, 268.
LYALL, DAVID: The Surgical Treatment of Intrinsic Knee Joint Lesions, 140.
LYONS, CHAMP: Problems of Infection and Chemotherapy, 894.

M

- MACCALLUM, JAMES D.: So-called Retroperitoneal Lipoma, 110.
MAGNUSON, PAUL B.: Textbook on Fractures. Reviewed by Walter Estell Lee, M.D., 320.
Malformations Implicating the Distal Spinal Cord, Surgical Treatment of the Congenital, 118.
MALLORY, TRACY B.: Pathology: With Special Reference to the Pulmonary Lesions, 865.
Management of the Coconut Grove Burns at the Massachusetts General Hospital, 801.

- MARBURY, WILLIAM BERRY: Spontaneous Rupture of the Urinary Bladder, 760.
MARIS, E. P.: The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, 348.
MCALPINE, A. D.: Trends in General Surgery, 297.
MCGUINNESS, A. C.: The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, 348.
MCLACHLIN, ANGUS D.: Spontaneous Rupture of a Normal Spleen, 476.
Mechanism of Shock in Intestinal Strangulation, 28.
Mechanisms of Head Injury, 562.
Megacolon Associated with Chronic Volvulus, Transverse, 786.
MELLORS, R. C.: Fluid, Protein and Electrolyte Alterations in Experimental Intestinal Obstruction, 39.
MERRITT, H. HOUSTON: Relation of Trauma to Syphilis of the Nervous System, 623.
Metabolic Observations, 937.
Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract. XII—The Glycerine Tolerance Test in Patients with Gastric Ulcer, 740.
Metabolism, Nitrogen, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.
Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, Pre- and Postoperative Use of a, 348.
Metastasis, Islet Cell Carcinoma of Pancreas, with, 437.
Method of Prolonged Ventricular Drainage, 798.
Mikulicz Pack, Intra-abdominal Use of, 256.
Miller-Abbott Tube, Improved Tip for, 159.
Minimal Criteria Required to Prove Causation of Traumatic or Occupational Neoplasms, 585.
Minimal Criteria Required to Prove Prima Facie Case of Traumatic Abortion or Miscarriage, 596.
Miscarriage, Minimal Criteria Required to Prove Prima Facie Case of Traumatic Abortion or, 596.
MOORE, FRANCIS D.: A Note on the Thrombophlebitis Encountered, 931.
MOORHEAD, JOHN J.: The Surgical Treatment of Intrinsic Knee Joint Lesions, 140.
MORGAN, ETHEL M.: The Pathology of Burns, 234.
MORITZ, ALAN R.: Mechanisms of Head Injury, 562.
Morphine and Antispasmodics, Administration in Biliary Colic, 207.
Mortality of Burns as Influenced by Rapid Tanning and by Transfusions, Early, 327.
MORTON, H. B.: Improved Tip for Miller-Abbott Tube, 159.
MULHOLLAND, JOHN H.: Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.

- Multilocular Scrous Cysts of the Round Ligament
Simulating Incarcerated Herniac, 216.
MUNRO, DONALD: The Late Effects of Craniocerebral Injuries, 544.
MUNSLOW, RALPH A.: A Method of Prolonged Ventricular Drainage, 798.
MUNTWYLER, E.: Fluid, Protein and Electrolyte Alterations in Experimental Intestinal Obstruction, 39.

N

- NATHANSON, IRA T.: Metabolic Observations, 937.
Neoplasms, Minimal Criteria Required to Prove Causation of Traumatic or Occupational, 585.
Nervous System, Relation of Trauma to Syphilis of the, 623.
Neuroblastoma, Intrathoracic, 93.
Neuropsychiatric Observations, 814.
Newborn, The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the, 348.
Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.
Note on Physical Therapy, 911.

O

- Obstruction, Fluid, Protein and Electrolyte Alterations in Experimental Intestinal, 39; In the Newborn, The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal, 348.
Occupational Neoplasms, Minimal Criteria Required to Prove Causation of Traumatic or, 585.
OPPENHEIMER, GORDON D.: Late Invasion of Bladder and Prostate in Cancer of the Rectum or Rectosigmoid Following Abdomino-Perineal Resection, 456.
Osteogenic Sarcoma of the Fibula, Traumatic Arteriosclerotic Aneurysm of the Tibial Artery Simulating an, 793.

P

- PACK, GEORGE T.: Metabolic Studies in Patients with Cancer of the Gastrointestinal Tract, XII. —The Glycerine Tolerance Test in Patients with Gastric Ulcer, 740.
Pack, Mikulicz, Intra-abdominal Use of, 256.
Palate, cleft, 1.
PARKER, DOUGLAS B.: Synopsis of Traumatic Injuries of the Face and Jaws. Reviewed by Henry Sage Dunning, M.D., 319.
Pathology of Burns, 234.
Pathology: With Special Reference to the Pulmonary Lesions, 865.
PAXTON, JOHN R.: The Intra-abdominal Use of the Mikulicz Pack, 256.
PAYNE, ROBERT L.: Transplantation of the Peritoneum During Suprapubic Cystotomy, 783.
PEARMAN, R. O.: *Cochliomyia Americana* Infestation in Man, 468.
Pedicule Flaps, Blood Circulation in, 692.
Peptic Ulcer, Indications for Jejunal Alimentation in the Surgery of, 387; Perforated, 710.

- Perforated Peptic Ulcer, 710.
Peritoneum During Suprapubic Cystotomy, Transplantation of the, 783; Effect of Sulfanilamide, Sulfathiazole, and Sulfadiazine Upon the, 677; Hyperesthesia of the Posterior (Objective Pain) in Appendicitis and Other Visceral Lesions, 735.
PETERSON, CHARLES W.: Cholesterosis of the Gallbladder, 450.
Physical Therapy, A Note on, 911.
Pilonidal Cyst, the Local Use of Buffered Sulfanilamide in Primary Closure, 191.
PITTMAN, HELEN: The Pulmonary Complications: A Clinical Description, 834.
Plasma Injection in Emergencies, a Light, Compact Unit for the Intravenous or Intra-osseous Injection of, 152.
Plasma Protein Variations in Surgical Patients, Study of, 52.
Pleural Cavity, The Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic *Staphylococcus Aureus* Infections of the, 670.
Postoperative Convalescence, Nitrogen Metabolism, Caloric Intake and Weight in, 512; Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, Pre- and, 348.
POTTER, PHILIP C.: Stenosing Tendovaginitis at the Radial Styloid. (De Quervain's Disease), 290.
POWERS, JOHN H.: Acute Appendicitis During the Later Decades of Life: Some Remarks on the Incidence of the Disease in a Rural Area, 221.
Preoperative Scrubbing in Abdominal Surgery, 535; 766.
Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, 348.
Pressure Dressing, Application of, to the Severely Frozen Limbs of Dogs, Prevention of Shock and Death by Immediate, 686.
Prevention of Shock and Death by Immediate Application of a Pressure Dressing to the Severely Frozen Limbs of Dogs, 686.
PRICE, ALISON H.: A Light, Compact Unit for the Intravenous or Intra-osseous Injection of Plasma in Emergencies, 152.
PRIESTLEY, JAMES T.: Gastrojejunal Colic Fistulae: With Special Reference to Associated Nutritional Deficiencies and Certain Surgical Aspects, 414.
Problem of Burn Shock Complicated by Pulmonary Damage, 915.
Problems of the Hospital Administration, 803; Of Infection and Chemotherapy, 894; Relating to Law and Surgery, Symposium on, 544.
Procedures in Rehabilitation of the Severely Burned, 903.
Prostate and Bladder in Cancer of the Rectum or Rectosigmoid Following Abdomino-Perineal Resection, Late Invasion of, 456.
Protein and Electrolyte Alterations in Experimental Obstruction, Fluid, 39; Variations in Surgical Patients, Study of Plasma, 52.
Protocols of Coconut Grove Disaster Patients

Admitted to the Massachusetts General Hospital, 959.
Pulmonary Complications: A Clinical Description, 834; Damage, The Problem of Burn Shock Complicated by, 915; Lesions, Pathology, with Special Reference to the, 865; Lesions, Roentgenologic Report of the, 841; Tuberculosis, Lobectomy for, 641.

R

Radial Styloid, Tendovaginitis, Stenosing at the (De Quervain's Disease), 290.
Radiologic and Surgical Features, Unusual, of Echinococcus Cyst of Lung, 268.
Rate of Epithelial Regeneration, 85.
Reading List of Entire Group of Medicolegal Articles Appearing Concurrently in Medical and Legal Journals under Editorship of Dr. Hubert W. Smith, 632.
Rectosigmoid or Rectum, Cancer of the, Following Abdomino-Perineal Resection; Late Invasion of Bladder and Prostate in, 456.
Rectum and Colon, Treatment of Postoperative Hypoproteinemia in Patients with Cancer of the, 748; Or Rectosigmoid, Cancer of the, Following Abdomino-perineal Resection; Late Invasion of Bladder and Prostate in, 456.
Reduction of the Mortality in the Surgical Management of Hyperthyroidism: The Use of the Short Interval Two-stage Lobectomy, 263.
REGAN, J. SUTTON: So-called Retroperitoneal Lipoma, 110.
Regeneration, Rate of Epithelial, 85.
Rehabilitation of the Severely Burned, Procedures in, 903.
Relation of Trauma to Diabetes, 607; Of Trauma to Syphilis of the Nervous System, 623.
Restoration of Blood Flow in Damaged Arteries, 481.
Resuscitation and Sedation of Patients with Burns Which Includes the Airway, 825.
Retroperitoneal Lipoma, So-called, 110.
RHINELANDER, FREDERIC W.: The Problem of Burn Shock Complicated by Pulmonary Damage, 915.
RHODES, C. P.: The Treatment of Postoperative Hypoproteinemia in Patients with Cancer of the Colon and Rectum, 748.
RHODES, JONATHAN E.: The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, 348; Review of Sulfanilamide and Related Compounds in General Practice, 319.
RITTER, JOSEPH A.: Intrathoracic Neuroblastoma, 93.
RIVER, LOUIS P.: Transverse Megacolon Associated with Chronic Volvulus, 786.
Roentgenologic Report of the Pulmonary Lesions, 841.
ROSENBLATT, MILLARD S.: Hydrometrocolpos in Infancy, 635.
Round Ligament, Multilocular Serous Cysts of, Simulating Incarcerated Herniae, 216.

ROURKE, G. MARGARET: Metabolic Observations, 937.
Rupture of a Normal Spleen, Spontaneous, 476; Of the Urinary Bladder, Urinary, 760.
Rural Area, Incidence of the Disease, Acute Appendicitis, During the Later Decades of Life; Some Remarks on, 221.

S

SALTZSTEIN, H. C.: Trends in General Surgery, 297.
SANES, S.: So-called Retroperitoneal Lipoma, 110.
Sarcoma, Osteogenic, of the Fibula, Traumatic Arteriosclerotic Aneurysm of the Tibial Artery Simulating a, 793.
SCHATZKI, RICHARD: Roentgenologic Report of the Pulmonary Lesions, 841.
SCOTT, JAMES V.: Pilonidal Cyst, the Local Use of Buffered Sulfanilamide in Primary Closure, 191.
Scrotum, Accessory Spleen in the, 754.
Scrubbing in Abdominal Surgery, Abdominal, 535.
SEALEY, W. C.: Reduction of the Mortality in the Surgical Management of Hyperthyroidism: The Use of the Short Interval Two-stage Lobectomy, 263.
Sedation and Resuscitation of Patients with Burns Which Include the Airway, 825.
SHALLOW, THOMAS A.: Congenital Cystic Dilatation of the Common Bile Duct, 355.
SHAPIRO, ALFRED L.: Multilocular Serous Cysts of the Round Ligament Simulating Incarcerated Hernia, 216.
SHELDON, WALTER HERMAN: Minimal Criteria Required to Prove Prima Facie Case of Traumatic Abortion or Miscarriage, 596.
Shock, Burn, The Problem of, Complicated by Pulmonary Damage, 915; And Death by Immediate Application of a Pressure Dressing to the Severely Frozen Limbs of Dogs, Prevention of, 686; In Intestinal Strangulation, Mechanism of, 28.
Short Interval Two-stage Lobectomy; Use of in Reduction of Mortality in the Surgical Management of Hyperthyroidism, 263.
Sigmoid, Substitution of the Urinary Bladder with a Segment of the, 106.
Skin, The Treatment of Congenital Hemangiomas of the, 134.
SMITH, BEVERLY CHEW: Acute Ileus, 427.
Social Service Activities, 809.
SOLOMON, H. C.: Relation of Trauma to Syphilis of the Nervous System, 623.
SOUTHWORTH, JAMES L.: Continuous Caudal Analgesia in Surgery, 321.
SOUTTER, LAMAR: A Note on the Blood Bank, 928.
Spinal Cord, The Surgical Treatment of the Congenital Malformations Implicating the Distal, 118; Fusion, Evolution of, 278.
SPINK, WESLEY W.: Sulfanilamide and Related Compounds in General Practice. Reviewed by J. E. Rhoads, M.D., 319.
Spleen in the Scrotum, Accessory, 754; Spontaneous Rupture of a Normal, 476.

- Spontaneous Rupture of a Normal Spleen, 476;
Rupture of the Urinary Bladder, 760.
- Staphylococcus Aureus Infections of the Pleural Cavity, The Local Effect of Sulfanilamide, Sulfathiazole and Sulfadiazine Upon Hemolytic, 670.
- STEFKO, PAUL L.: Restoration of Blood Flow in Damaged Arteries, 481.
- Stenosing Tendovaginitis at the Radial Styloid. (De Quervain's Disease), 290.
- STOUT, ARTHUR PUROY: Review of Atlas of Ovarian Tumors, by, 639.
- Strangulation, Mechanism of Shock in Intestinal, 28.
- STRAUSS, ABRAHAM: Congenital Atresia of the Common Bile Duct, 723.
- STRODE, J. E.: Biliary Dyskinesia from the Surgical Viewpoint, 198.
- STUCK, WALTER G.: Clinical Uses of Vitallium, 772.
- Study of Plasma Protein Variations in Surgical Patients, 52.
- Substitution of the Urinary Bladder with a Segment of Sigmoid, 106.
- Sulfadiazine, Sulfanilamide, and Sulfathiazole, The Effect of, Upon the Peritoneum, 677; Sulfadiazine, Sulfathiazole, and Sulfanilamide, The Local Effect of, Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670.
- Sulfanilamide, Buffered; Local Use in Primary Closure of Pilonidal Cyst, 191; And Related Compounds in General Practice. Reviewed by J. E. Rhoads, M.D., 319; Sulfathiazole and Sulfadiazine, The Local Effect of, Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670; Sulfathiazole and Sulfadiazine Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, The Local Effect of, 670; Sulfathiazole, and Sulfadiazine, The Effect of, Upon the Peritoneum, 677.
- Sulfathiazole, Sulfadiazine, and Sulfanilamide, The Effect of, Upon the Peritoneum, 677; Sulfadiazine, and Sulfanilamide, The Local Effect of, Upon Hemolytic Staphylococcus Aureus Infections of the Pleural Cavity, 670.
- Surgical Management of Hyperthyroidism, Reduction in the Mortality of: The Use of the Short Interval Two-stage Lobectomy, 263; Treatment of Congenital Malformations Implicating the Distal Spinal Cord, 118; Treatment of Intrinsic Knee Joint Lesions, 140; Treatment of Tophaceous Gout, 161; Viewpoint of Biliary Dyskinesia, 198.
- Surgery, Continuous Caudal Analgesia in, 321; General, Trends in, 297.
- Surface Burns, Treatment of the, 885.
- Symposium on Problems Relating to Law and Surgery, 544.
- Syphilis of the Nervous System, Relation of Trauma to, 623.
- Tanning, Rapid, Early Mortality of Burns as Influenced by Transfusions and, 327.
- Tendovaginitis, Stenosing at the Radial Styloid. (De Quervain's Disease), 290.
- Test in Patients with Gastric Ulcer, Glycerine Tolerance. Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract, 740.
- Therapy, A Note on Physical, 911.
- Thoracoplasty, First stage, 315.
- THORSTAD, M. J.: Trends in General Surgery, 297.
- Thrombophlebitis Encountered, A Note on the, 931.
- Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, Traumatic Arteriosclerotic Aneurysm of the, 793.
- TIMONEY, FRANCIS X.: Perforated Peptic Ulcer, 710.
- Tip for Miller-Abbott Tube, Improved, 159.
- TOCANTINS, L. M.: A Light, Compact Unit for the Intravenous or Intra-osseous Injection of Plasma in Emergencies, 152.
- Tophaceous Gout, the Surgical Treatment of, 161.
- Total Gastrectomy for Cancer, 183.
- Towel Clip, An Improved, 637.
- Transfusions, Early Mortality of Burns as Influenced by Rapid Tanning and by, 327.
- Transplantation of the Peritoneum During Suprapubic Cystotomy, 783.
- Transverse Megacolon Associated with Chronic Volvulus, 786.
- Trauma, relation of, to Syphilis of the Nervous System, 623; To Diabetes, Relation of, 607.
- Traumatic Abortion or Miscarriage, Minimal Criteria Required to Prove Prima Facie Case of, 596; Arteriosclerotic Aneurysm of the Tibial Artery Simulating an Osteogenic Sarcoma of the Fibula, 793; Injuries of the Face and Jaws. Reviewed by Henry Sage Dunning, M.D., 319; Or Occupational Neoplasms, Minimal Criteria Required to Prove Causation of, 585.
- Treatment of Congenital Hemangiomata of the Skin, 134. Of Gout, Tophaceous, Surgical, 161; Of Intrinsic Knee Joint Lesions, Surgical, 140; Of Postoperative Hypoproteinemia in Patients with Cancer of the Colon and Rectum, 748; Surgical, of Tophaceous Gout, 161; Of the Surface Burns, 885.
- Trends in General Surgery, 297.
- Tube as an Aid in the Surgical Treatment of Duodenal Obstruction in the Newborn, The Pre- and Postoperative Use of a Metal-Tipped Gastroduodenal, 348.
- Tube, Miller-Abbott, Improved Tip for, 159.
- Tuberculosis, Lobectomy for Pulmonary, 641.
- Two-stage Lobectomy, Use of the Short Interval in Reduction of the Mortality in the Surgical Management of Hyperthyroidism, 263.
- Two-way Valve, a New, 313.
- WATKINS, ARTHUR L.: A Note on Physical Therapy, 911.
- WILSON, HILDEGARDE: Metabolic Observations, 937.

U

- Ulcer, Gastric, Glyccrine Tolerance Test in Patients with Metabolic Studies in Patients with Cancer of the Gastro-intestinal Tract, 740; Indications for Jejunal Alimentation in the Surgery of Peptic, 387; Intractable Duodenal, 498; Perforated Peptic, 710.
Umbilical Discharge in Acute Appendicitis, 473.
Urinary Bladder, Spontaneous Rupture of the, 760.
Unit for Intravenous or Intra-osseous Injection of Plasma in Emergencies, 152.

V

- Valve, a New Two-way, 313.
VAN BEUREN, FREDERICK T.: Acute Ileus, 427.
Vater, Cyst of the Ampulla of, 728.
VENABLE, CHARLES S.: Clinical Uses of Vitallium, 772.
Ventricular Drainage, Method of Prolonged, 798.
VINCI, VINCENT J.: Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.
Visceral Lesions, Hypcresthesia of the Posterior Peritoneum (Objective Pain) in Appendicitis and other, 735.
Vitallium, Clinical Uses of, 772.

- Volvulus, Transverse Megacolon Associated with Chronic, 786.

W

- WAGNER, FREDERICK B.: Congenital Cystic Dilatation of the Common Bile Duct, 355.
WALTERS, C. E.: Empyema Complicated by Broncho-esophagopleural Fistula, 100.
WARD, CHARLES S., JR.: Atresia of the Duodenum, 718.
WARREN, SHIELDS: Minimal Criteria Required to Prove Causation of Traumatic or Occupational Neoplasms, 585.
WEINSTEIN, ALBERT: Cyst of the Ampulla of Vater, 728.
WOOD, GEORGE W.: Review of Ophthalmology and Otolaryngology: Military Surgical Manuals II, by, 640.
WOOLLEY, PAUL V. JR.: Hydrometrocolpos in Infancy, 635.
WRIGHT, ARTHUR M.: Nitrogen Metabolism, Caloric Intake and Weight Loss in Postoperative Convalescence, 512.

Z

- ZUELZER, WOLF W.: Echinococcus Cyst of Lung Exhibiting Unusual Radiologic and Surgical Features, 268.

S.M.S. MEDICAL COLLEGE
LIBRARY, JAIPUR.